UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK
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TEVA PHARMACEUTICALS USA, INC., TEVA PHARMACEUTICALS INDUSTRIES LTD., TEVA NEUROSCIENCE, INC. and YEDA RESEARCH AND DEVELOPMENT CO. LTD.,

Plaintiffs,

v. 08-CV-7611 (BSJ)

SANDOZ, INC., SANDOZ INTERNATIONAL GMBH, NOVARTIS AG, and MOMENTA PHARMACEUTICALS, INC.,

Defendants.

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TEVA PHARMACEUTICALS USA, INC., TEVA PHARMACEUTICALS INDUSTRIES LTD., TEVA NEUROSCIENCE, INC. and YEDA RESEARCH AND DEVELOPMENT CO. LTD.,

Plaintiffs,

v. 09-CV-8824 (BSJ)

MYLAN PHARMACEUTICALS INC., MYLAN INC., NATCO PHARMA LTD.,

Defendants. Non-Jury Trial

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New York, N.Y.
September 8, 2011
9:35 a.m.

Before:

HON. BARBARA S. JONES,

District Judge

APPEARANCES

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SHANNON M. BLOODWORTH, ESQ.
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ALSO PRESENT: CORT CHASE, Litigation Support

THE COURT: Good morning. Please be seated.

Dr. Grant.

THE WITNESS: Good morning.

THE COURT: Were there some issues that anyone wanted to raise, Mr. Skilton?

MR. SKILTON: Yes. Thank you, your Honor. Counsel have been working cooperatively planning the case down to the second if we can. And yesterday we were talking about the conclusion of plaintiff's case, and I think, as I understand it from Mr. Hashmall, it's possible that he'll end early on Friday earlier than the end of the day. And we had planned, we being the defendants, had planned to start our case for about ten days next Tuesday morning, and wanted to alert the Court that it's possible that there will be some dark time, should the Court permit, in order for us to properly get ready for to present our case. And I believe that's agreeable to counsel.

THE COURT: Mr. Hashmall?

MR. HASHMALL: Yes, your Honor.

THE COURT: You think you're going to be done tomorrow?

MR. HASHMALL: It's possible. We don't know the lengths of the cross.

THE COURT: I see.

MR. HASHMALL: And I think, and I think a little uncertain about today. I believe we're ending at 3:45 today?

THE COURT: There's a court session, which is a remembrance of 9/11 at 4:00 o'clock, and I have a civil matter that I have to handle on a class action, they're coming in at 3:00, so we're going to adjourn at 3:00.

MR. HASHMALL: So it's very possible that we will take up most of the day Friday, but again a little uncertain because we're basing it on what we know to be the anticipated lengths of our directs, but we don't know the lengths of the cross. So Mr. Skilton said if we end, you know, at some point before 5:00 o'clock tomorrow, we would have no objection to adjourning at that point and beginning.

THE COURT: Okay. I have no objection either, Mr. Skilton.

MR. SKILTON: Thank you, your Honor.

THE COURT: So you'll be ready for Tuesday morning then.

MR. SKILTON: Thank you, your Honor.

THE COURT: Okay, thanks.

MR. HASHMALL: And, your Honor, just to I think there's one point we hadn't quite clarified at the pretrial conference. We had discussed whether plaintiffs would be putting on --

THE COURT: Oh, yes.

MR. HASHMALL: And I think, as your Honor may know, we are just putting on infringement now and then, and then next

week the defendants will start their non-infringement and their invalidity, then we'll put on our invalidity response after defendants rest.

THE COURT: Right. I did see that, but thank you. And that's clear with everyone?

MR. DOYLE: It is, your Honor.

THE COURT: Great, all right. Then continue with direct.

MR. JAMES: Thank you, your Honor.

THE COURT: You're welcome.

GREGORY GRANT,

called as a witness by the plaintiff,

having been previously sworn, testified as follows:

DIRECT EXAMINATION

BY MR. JAMES:

Q. Dr. Grant, when we left off yesterday afternoon, we were going to turn to the issue of the Mylan and Natco ANDA products. Dr. Grant, have you reviewed the Mylan and Natco submissions to the FDA regarding their ANDA product?

A. Yes, I have.

Q. And have you formed an opinion as to whether the generic Copaxone proposed by Mylan and Natco meets the average molecular weight limitation of the asserted claims of the patents?

A. Yes, I have. It's my opinion that the Copaxone product

that Mylan and Natco will produce does meet claims of the patents.

Q. Now Dr. Grant, let's turn to plaintiff's trial Exhibit 318 in your binder?

A. I'm afraid -- oh, there it is. I'm sorry.

MR. JAMES: For the record, your Honor, this is one of those exhibits that we will offer into evidence in its unredacted form, but will provide a public version that's been redacted by Mylan and Natco's counsel.

THE COURT: All right and under that circumstance, is there any objection?

MS. BLOODWORTH: No, your Honor.

THE COURT: All right, then if it hasn't already been admitted --

MR. JAMES: I don't think it has been.

THE COURT: All right, PTX-318 is admitted.

(Plaintiff's Exhibit PTX-318 received in evidence)

Q. Dr. Grant, did you rely on this document in forming your opinions in this case?

A. Yes, I did.

Q. Let's look at page 107 toward the bottom paragraph 4A. And, Dr. Grant, if you would, the sentence in 4A that begins, peak average molecular weight, could you read that into the record, please?

A. It says, "peak average molecular weight of the sponsor's

product was within the 5,000 to 9,000 dalton range specified in the approved labeling for Copaxone."

Q. And who do you understand the sponsor to be there?

A. I understand that to be Mylan and Natco.

Q. And what do you understand that sponsor's product to be?

A. I understand it to be Copaxone, co-polymer-1.

Q. Do you understand Mylan's, Mylan and Natco's glatiramer acetate product to be co-polymer-1?

A. Yes, I do.

Q. Do you understand that their product is non-uniform with respect to molecular weight and sequence?

A. Yes, it is.

Q. Now, do you know whether Mylan and Natco have a specification for the peak average molecular weight of their product?

A. Yes. It's 5,000 to 9,000 daltons.

Q. And did you look at the data to see if those data demonstrate that the peak molecular weight of the product was within the specification of 5,000 to 9,000 daltons?

A. Yes, I did.

Q. And what did you conclude?

A. I concluded that it was within that specification.

Q. Does the ANDA indicate what types of calibrations standards were used?

A. Yes, it does.

Q. And what were they?
A. They were synthetic polypeptides.
Q. What types of synthetic polypeptides?
A. They were synthetic polypeptides that were designed with the same four amino acids as co-polymer-1 and have the same -- designed to have the same size to molecular weight relationship as co-polymer-1.
Q. Thank you, Dr. Grant. Now, if you could turn to page 117 in your binder, please, page 117 of plaintiff's Exhibit 318?
A. Okay.
Q. If you could bring up the first full paragraph, please.

Dr. Grant, could you read the highlighted sentence into the record, please?
A. "In addition, each technique yielded Mp values for the GMA lots and Copaxone that were within the 5,000 to 9,000 dalton range specified in the approved labeling for Copaxone.
Q. And what does that convey to you, Dr. Grant?
A. That conveys to me that the peak average molecular weights of their GMA lots were within the range of 5,000 to 9,000 daltons, and thus met the limitations of the patent.
Q. Okay, thank you. Could you turn to page MYL-111, please? If you could pull the two paragraphs at the bottom, please.

Dr. Grant, we highlighted a sentence at the bottom of the first paragraph on the screen. Could you read that, please?

A. Starting with it is, therefore?
Q. Yes.
A. "It is, therefore, imperative in SEC to have a good set of calibration standards in order to obtain accurate results. That is, the standards should be chemically as similar as possible to the polymer of interest."
Q. Do you agree with that?
A. Yes, I do.
Q. And could you explain what that means?
A. Well, it's just another way of saying what I've been saying both yesterday and today; that in order to get an accurate molecular weight of the polymer of interest, you need to have a good set of standards that are appropriate for that purpose and that have the same size to molecular relationship as the polymer does.
Q. And could you read the next sentence that begins, for this reason, into the record, please?
A. "For this reason, the calibration standards used for the SEC UV. and SEC RI analyses of GMA and Copaxone were polypeptides consisting of the same four amino acids present in Copaxone, alamine, glutamic acid, tyrosine and lysine.
Q. Dr. Grant, do you have an opinion as to whether Mylan used appropriate calibration standards for its molecular weight determinations?
A. Yes, I do. I believe that they did use appropriate

standards for the calibrations.
Q. And could you explain the basis for that opinion?
A. Well, basis for it is that they essentially say so in their ANDA. And what I've been able to read in the ANDA, I've come to the conclusion that they have, indeed, done everything that they needed to do to assure that they had appropriate standards.
Q. Now, did Natco perform a molecular weight analysis on the product?
A. Yes, they did.
Q. Could you turn to tab PTX-330 in your binder, please? Dr. Grant, can you identify plaintiff's trial Exhibit 330?
A. Yes. It's part of their ANDA. Its actually from Natco, and it's a list of specifications for their glatiramer acetate.
Q. Did you review this document in preparing your opinions in this case?
A. Yes, I did.
Q. Did you rely on this document?
A. Yes, I did.
MR. JAMES: Your Honor, we would offer into evidence plaintiff's trial exhibit 330?
THE COURT: Any objection?
MS. BLOODWORTH: No, your Honor.
THE COURT: All right, admitted.
(Plaintiff's Exhibit 330 received in evidence)

Q. Let's look at pages 765 to 766, Dr. Grant.
A. Okay.
Q. What do those pages show?
A. These pages show a test method that was used to determine the molecular weight distribution of the glatiramer acetate.
Q. Does the test method say what the specification was that they were trying to hit for there glatiramer acetate product?
A. Yes. It says between 5,000 and 9,000 daltons.
Q. If you look under chromatographic conditions on page 765; you see that?
A. Yes.
Q. Do they indicate what type of column they used for their molecular weight analysis?
A. Yes. They used a Superose 12 column.
Q. And, Dr. Grant, was Natco's molecular weight analysis carried out on appropriately calibrated suitable gel filtration column?
A. Yes, it was. Superose 12 is the same column that's listed in the patents in suit. So that certainly is a suitable filtration column.

As I've explained just recently, everything that I've seen suggests to me that they are using appropriate standards.

Q. Dr. Grant, can you turn to page, I'm sorry, excuse me, plaintiff's trial Exhibit 325 in your binder, please?
A. Okay.

Q. Can you identify that document, Dr. Grant?
A. This is another portion of the ANDA. It's information from Natco, and it contains a list of batch analysis.
Q. Is this a document that you relied on in forming your opinions in this case?
A. Yes, it is.
MR. JAMES: Your Honor, we would offer into evidence plaintiff's trial exhibit 325?
THE COURT: Any objection?
MS. BLOODWORTH: Just the same confidentiality objections, your Honor.
THE COURT: All right. It's admitted.
(Plaintiff's Exhibit 325 received in evidence)
Q. Does plaintiff's trial Exhibit 325 provide certificates of analysis for the drug substance that Natco provided to the FDA?
A. Yes, it does. On the page that I'm looking at, 1050, there is a certificate of analysis of glatiramer acetate.
Q. Pull that up. This is a certificate of analysis for which batch, Dr. Grant?
A. This is lot number GMA 00109.
Q. And does the certificate of analysis for the GMA 00109 batch provide a peak molecular weight value?
A. Yes, it does.
Q. And where is that found?
A. That's found in row seven, titled molecular weight

distribution.
Q. And what is the value provided for that lot?
A. It gives a value of 6,445.
Q. Okay. Dr. Grant, let's turn now to Mylan 1068 in the same exhibit.
A. Okay.
Q. Can you identify that document?
A. Yes. This is a another certificate of analysis from Natco Pharma concerning the lot number GMA 00209 of glatiramer acetate.
Q. And what molecular weight did Natco report for that batch?
A. 6,431.
Q. And what type of molecular weight was that?
A. That's a peak average molecular weight.
Q. Could you turn now to Mylan 1079 through 1080?
A. Okay.
Q. Dr. Grant, can you identify those two pages?
A. Yes. This is another certificate of analysis from Natco Pharma concerning lot number GMA 00309 for glatiramer acetate.
Q. And what is the molecular weight in Natco reported for that lot of glatiramer acetate?
A. 6,718.
Q. Dr. Grant, let's turn to plaintiff's trial Exhibit 300 in your binder.
A. Okay.

Q. Can you identify plaintiff's trial exhibit 300?
A. Yes. This is a certificate of analysis from Gland Pharma and it concerns batch number WV. 01 of glatiramer acetate injection.
Q. What is glatiramer acetate injection?
A. Glatiramer acetate injection is their drug product.
Q. And, Dr. Grant, did you review this document in forming your opinions in this case?
A. Yes, I did.
Q. And did you rely on this document?
A. Yes, I did.
MR. JAMES: Your Honor, we would offer into evidence plaintiff's trial exhibit 300.
THE COURT: Any objection?
MS. BLOODWORTH: Just the same confidentiality, your Honor.
THE COURT: All right. 300 is admitted.
(Plaintiff's Exhibit 300 received in evidence)
Q. Dr. Grant, what is the molecular weight reported for drug product batch WB 901?
A. 6,280.
Q. Dr. Grant, please turn to plaintiff's trial Exhibit 312 in your binder. Can you identify that?
A. This is a certificate of analysis from Gland Pharma concerning batch number WV 902, glatiramer acetate injection.

Q. Did you rely on this document in forming your opinions, Dr. Grant?
A. Yes, I did.
MR. JAMES: Your Honor, we would offer into evidence plaintiff's trial Exhibit 312.
THE COURT: Any objection?
MS. BLOODWORTH: Same confidentiality, your Honor.
THE COURT: All right, 312 is admitted.
(Plaintiff's Exhibit 312 received in evidence)
Q. Dr. Grant, what is the molecular weight reported for WV 902?
A. 6,358.
Q. And, finally, Dr. Grant, if you could turn to plaintiff's trial exhibit 313. Can you identify that document?
A. This is a certificate of analysis from Gland Pharma concerning batch number WV 903.
Q. Did you review and rely on this document in rendering your opinions in this case, Dr. Grant?
A. Yes, I did.
MR. JAMES: Your Honor, we would offer into evidence plaintiff's trial Exhibit 313.
THE COURT: All right.
MS. BLOODWORTH: Same confidentiality, your Honor.
THE COURT: All right. Admitted.
(Plaintiff's Exhibit 313 received in evidence)

Q. Dr. Grant, what is the peak molecular weight provided for batch WV 903?
A. 6,036.
Q. Now, Dr. Grant, have you prepared a slide that summarizes the peak molecular weight values reported in the ANDA for the various lots of Mylan's glatiramer acetate drug substance and drug product?
A. Yes, I have.
Q. Let's look at the slide.
I think we want to go forward a few slides, John.
Dr. Grant, could you explain what's shown on this slide please?
A. This slide shows a summary of the molecular weights of Mylan's drug product and drug substance that we just reviewed. On the top, on the left-hand side under lot it gives the lot numbers that were reviewed, and on the right-hand side it gives the peak average molecular weight from the certificate of analysis. And on the bottom is the same information for the drug product giving the various different lot numbers and the molecular weights, the peak average molecular weights that we determined from the certificates of analysis.
MR. JAMES: For the record, Dr. Grant is testifying about slide number 44.
Q. Let's go to the next slide. Dr. Grant, have you made a determination as to which of the average molecular weight claim

limitations the Mylan and Natco products literally satisfy?
A. Yes. In my opinion the Natco and Mylan products literally satisfy all of the about five to nine kilodalton claim limitation, all of them satisfy that.
Q. And, Dr. Grant, have you made a determination as to which of the lots satisfy the claim limitation of average molecular weight about four to about nine kilodaltons?
A. Yes. In my opinion, all of the lots also satisfy that limitation.
Q. Dr. Grant, finally, have you made an analysis and formed an opinion as to which of the lots satisfy the ample molecular weight 6.25 to 8.4 kilodalton limitation?
A. Yes. In my opinion, again all of the lots satisfy that, with the exception of the last one.
Q. And, Dr. Grant, do you have an opinion as to whether if Mylan and Natco followed the process that's outlined in their ANDA, whether the resulting co-polymer-1 product will meet the average molecular weight limitations of the asserted claims of the patents-in-suit?
A. Yes. In my opinion if Mylan and Natco follow the procedure outlined in their ANDA, their drug product will meet all of the claims of the average molecular weights of the patents-in-suit.
Q. Thank you. Dr. Grant, I'd like to turn now to the co-polymer-1 molar fraction limitations. Did you analyze whether Mylan and Natco's glatiramer acetate product meets the

co-polymer-1 molar fraction limitations of the claims?
A. Yes, I did.
Q. Did you receive electronic data to determine the co-polymer-1 molar factions from Mylan glatiramer acetate?
A. Yes, I did.
Q. Can you explain what form they were provided to you in?
A. It was provided on CD with empower software.
Q. And can you give us an idea of the volume of data you were provided with?
A. There was a large amount of data, when we extracted it from the CD and put it into an excel spread sheet. I don't know the exact number of pages, but there were very large number.
Q. And did you do a calculation to determine whether the Mylan Natco proposed drug substance meets the molecular weight that co-polymer-1 molar fraction limitation of the claims?
A. Yes, I did.
Q. Did you work with anybody to perform your calculations, Dr. Grant?
A. Yes. As with the other drug substance, I worked with Dr. Paul Winter of Chemir Laboratories in St. Louis.
Q. And did Dr. Winter do any independent calculations on the data?
A. No. He only did what I instructed him to do.
Q. And, Dr. Grant, what were the results of your calculations?
A. The results of my calculation were that I concluded that

all of the lots that we analyzed, that the claim limitations of molar factions between two and 20 kilodaltons and lower fraction above 40 kilodaltons.

Q. Dr. Grant, we're looking at slide 46 on the screen. Is this a slide that you prepared?

A. Yes, it is. It's a summary of the results of my analysis.

MR. JAMES: Your Honor, plaintiffs would offer slide 46 under Rule 1006 as a summary of the data that and calculations that Dr. Grant did.

THE COURT: Any objection?

MS. BLOODWORTH: No objection, your Honor.

THE COURT: All right, admitted.

(Plaintiff's Exhibit 46 received in evidence)

Q. Dr. Grant, with respect to the batches that are shown on this slide -- if we go to the next slide, and if we could go forward one -- which of the batches that you analyzed, Dr. Grant, had over 75 percent of the copolymers on a molar fraction basis between two and 20 kilodaltons?

A. All of the batches met that limitation.

Q. Dr. Grant, which of the batches that you analyzed had less than 2.5 percent on a molar fraction basis copolymers above 40 kilodaltons?

A. In my opinion, all of the batches met that limitation.

Q. And, Dr. Grant, which of the batches that you analyzed had both over 75 percent on the molar fraction basis copolymers

between two and 20 kilodaltons and less than 2.5 percent over 40 kilodaltons?

A. Again, in my opinion, all of the batches met that limitation also.

Q. And finally, Dr. Grant, in your opinion, which of the batches that you analyzed had both over 75 percent on a molar fraction basis copolymers between two and 20 kilodaltons and less than 5 percent copolymers over 40 kilodaltons?

A. In my opinion, all of the batches met that limitation.

Q. And, Dr. Grant, do you have an opinion as to whether if Mylan and Natco used the this synthetic process as described in their ANDA, that the resulting batches will meet the co-polymer-1 molar fraction limitations of the asserted claims?

A. Yes. In my opinion, if Mylan and Natco used the process described in their ANDA, the batches, their product will meet all of the limitations that are described in the claims.

Q. Now, Dr. Grant, let's turn now to the TFA co-polymer-1 molar fraction terms. Does the synthetic route that's described in the Mylan and Natco ANDA, does that make use of the trifluoracetyl co-polymer-1 intermediate?

A. Yes, it does.

Q. And were you able to calculate the molar fraction of the Mylan and Natco trifluoracetyl co-polymer-1 intermediate?

A. Yes, I was.

Q. Could you explain briefly how you did that calculation?

A. Yes, I did it really in the same way that I did the calculation that we discussed yesterday. And in brief we know that the TFA is on all of the lysine residues. And we know that TFA has a discreet molecular weight. And from the information in the ANDA, we also know the mole percentage of lysine in the product, and that allows us then to do a simple calculation to get a conversion factor where we can convert the molecular weight of co-polymer-1 to the molecular weight of TFA co-polymer-1.

Q. And did you create a slide, Dr. Grant, that shows the results of your calculations on the Mylan and Natco product?

A. Yes, I did.

Q. Let's look at the next slide. Dr. Grant, could you explain what's shown on slide 50, please?

A. Yes. Again, this is a summary of the results of my calculation. On the left-hand side it shows three batches of trifluoracetyl co-polymer-1, corresponding to the sample. And on the right it has percent, TFA molar fraction between two and 20 kills kilodaltons and the results that are expressed as percentage.

MR. JAMES: Your Honor, plaintiffs would offer slide 50 into evidence under Rule 1006 as a summary of the calculations that Dr. Grant performed.

MS. BLOODWORTH: No objection.

THE COURT: Admitted.

(Plaintiff's Exhibit 50 received in evidence)

Q. Dr. Grant, do you have an opinion as to which of the batches that you analyzed demonstrated that the Sandoz, excuse me -- Mylan and Natco product would use a trifluoracetyl co-polymer-1 that meets this limitation of having over 75 percent of its molar fraction between the molecular weight range of two and 20 kilodaltons?

A. Yes. It's my opinion that their product would meet this limitation.

Q. And, Dr. Grant, do you have an opinion as to whether if Mylan and Natco were to carry out the process described in their ANDA, whether the synthetic route would use a trifluoracetyl co-polymer-1 intermediate that meets this claim limitation?

A. Yes, in my opinion it would.

Q. Dr. Grant, I'd like to summarize a little bit what we talked about. Have you created slides that summarize your opinions as to whether the Sandoz and Mylan ANDA products will meet all of the molecular weight limitations of the asserted claims of the patents in suit?

A. Yes, I have.

Q. Look at the next slide, please. Dr. Grant, could you explain to the Court what's shown on slide 52?

A. Yes. This slide shows the three molecular weight limitations from the patents-in-suit, and again shows the

claims where they're found, the about five to nine kilodalton limitation is found in claim one of the '808 patent, and the claim one of the '589 patent. The about four to about nine kilodaltons is in claims one and six of the '847 patent. Claims 1, 8, 9, 12, 23, 30 and 31 of the '539 patent, and then the 6.25 to 8.4 kilodaltons claim is in claim ten, limitations in claim ten of the '539 patent.

Q. And, Dr. Grant, what types of molecular weight limitations are these shown in the slide?

A. These are peak average molecular weights.

Q. And, Dr. Grant, what is your opinion as to whether or not the Sandoz and Mylan ANDA products will meet those average molecular weight limitations?

A. My opinion is that the Sandoz and Mylan products will meet all of those limitations.

Q. Dr. Grant, have you prepared as a summary slide with respect to the co-polymer-1 molar fraction limitation?

A. Yes.

Q. Let's look at the next slide. Could you explain what's shown on slide 53 to the Court, please?

A. Yes. Again, I've listed the limitation in gray. Over 75 percent between two and 20 kilodaltons are found in claims one to three of the '430 patent, less than 2.5 percent above 40 kilodaltons are in claims 8 and 30 of the '539 patent; over 75 percent between two and 20 kilodaltons and less than

2.5 percent over 40 kilodaltons are in claims 9, 10, 31 of the '539 patent, and claim 8 of the '098 patent; and then over 75 percent between two and 20 kilodaltons, and less than 5 percent over 40 kilodaltons, is in claim one of the '476 patent, claim 1 of the 161 patent and claim 1 of the '098 patent.

Q. Dr. Grant, have you formed an opinion as to whether the Sandoz and Mylan ANDA products will meet those co-polymer-1 molar fraction limitations in the claims you've outlined in that slide?

A. Yes. In my opinion, both Sandoz and the Mylan products will meet those limitations.

Q. And finally, Dr. Grant, have you created a summary slide with respect to the TFA co-polymer-1 molar fraction limitation?

A. Yes, I have.

Q. Let's look at the next slide. Dr. Grant, could you explain what's shown on slide 54, please?

A. This shows the one limitation, trifluoracetyl co-polymer-1 having over 75 percent of its molar fraction within the molecular weight range from about two kilodaltons to about 20 kilodaltons. It shows that this is found in claims 1 to 3 of the '430 patent, claim 1 of the 476 patent, and claim 1 of the '161 patent.

Q. Dr. Grant, have you formed an opinion as to whether the Sandoz and Mylan ANDA products will meet that trifluoracetyl

co-polymer-1 molar fraction limitation?
A. Yes. In my opinion, both the Sandoz and the Mylan products will meet that limitation.
Q. Dr. Grant, thank you very much. I have no further questions.
THE COURT: All right.
MR. ACKER: Thank you, your Honor. Just one second to get some binders.
THE COURT: Sure.
MR. ACKER: May I approach, your Honor?
THE COURT: Yes.
CROSS EXAMINATION
BY MR. ACKER:
Q. Good morning, Dr. Grant.
A. Good morning.
Q. We haven't had the pleasure of meeting. My name is Eric Acker and I represent Sandoz and Momenta defendants. Do you understand that?
A. Yes, I do.
Q. I'd like to start with a few questions regarding your qualifications. Yesterday you testified that universal calibration was a technique known to those skilled in the art in 1994 to calibrate an SEC column, correct?
A. Yes.
Q. Before you were retained as an expert in this case, how

many times did you, yourself, use universal calibration to calibrate an SEC column?
A. I've not used universal calibration.
Q. So in the 25 years of your scientific research between 1975 and when you graduated with a Ph.D., until you were retained as an expert in this case, you never used universal calibration once, correct?
A. That's correct. I didn't have a need for it.
Q. And you're also, you're not an expert in universal calibration, is that correct?
A. I've read literature on it. I understand it completely.
Q. But you're not an expert?
A. I'm not sure what you mean by an expert.
Q. Well, are you an expert in universal calibration?
A. I understand the concept of the theory and the practice of universal calibration.
Q. Is your testimony here today you are an expert in universal calibration?
A. I've not used universal calibration. I mean, if you're defining an expert in universal calibration as somebody who has performed the method in the laboratory, I've not done that.
Q. So you wouldn't consider yourself to be an expert in it?
A. If that's the way you define it.
Q. Since earning your Ph.D. in 1975, you worked at the Washington University School of Medicine the entire time,

correct?
A. Yes.
Q. You've never worked full-time in a drug development, in drug development for a pharmaceutical company, is that correct?
A. That's correct.
Q. And you mentioned yesterday Superose 12 SEC column that is referenced in asserted patents, it's made by a company called Pharmacia, correct?
A. At one time it was. I think the name of the company is changed.
Q. At the time the patents issued in 1999, were filed in 1994 it was made by a company called Pharmacia, correct?
A. I believe so.
Q. Have you ever been retained by Pharmacia to develop a laboratory course and lecture for its employees on SEC techniques?
A. No.
Q. Have you at your laboratory, Washington University, has it ever been used as a beta test site for a new Pharmacia SEC column?
A. No.
Q. Have you ever managed a protein manufacturing group at a major biotech company?
A. No, I have not.
Q. Have you ever developed standards for SEC calibration that

were adopted by the National Institutes of Health?
A. No.
Q. And you're not the inventor on any patents, correct?
A. That's correct.
Q. And prior to being retained as an expert in this case, you had never been involved in any scientific research involving co-polymer-1, correct?
A. I have not worked with co-polymer-1.
Q. And so before being retained in this case, you had never been involved in any attempt to determine the molecular weight of co-polymer-1, correct?
A. That's correct.
Q. And none of your articles or scientific publications or lectures have anything to do with co-polymer-1, correct?
A. That's correct.
Q. Now, when you set out to determine whether or not, in your opinion, there was infringement in this case, you looked at Sandoz ANDAs, correct; that's how you did your analysis?
A. I looked at portion of the ANDAs that dealt with molecular weight.
Q. And you had access to samples of Sandoz proposed product, correct?
A. I don't know that I did.
Q. Well, did you make any effort to actually test Sandoz's product as opposed to just reviewing Sandoz's ANDA?

A. No, I didn't.
Q. Did you ask counsel for Teva whether you would have access to those samples so that you could actually test the product as opposed to just reviewing the ANDAs to reach your opinions?
A. No, I didn't.
Q. So you relied just on molecular weight information listed in Sandoz's ANDA to come to your opinions, right?
A. That's correct.
Q. And as a result, your infringement opinion necessarily is based on the techniques used in the molecular weights obtained in Sandoz's ANDA, right?
A. My opinion is based on what they reported.
Q. And what they reported is based on the techniques that were used in the ANDA to get those molecular weights, right?
A. They used the techniques that they reported, yes.
Q. In the ANDAs, there are molecular weights calculated in several different ways, correct?
A. What do you mean by several different ways?
Q. Well, as you testified, the numbers that you relied on were calculated using SEC and peptides standards, correct?
A. Yes.
Q. But also in Sandoz's ANDA there are molecular weights calculated using SEC calibrated with protein standards, correct?
A. I believe so.

Q. And the molecular weights for the different batches of co-polymer-1 in the Sandoz ANDA are different, depending on whether the SEC column was calibrated with protein standards or with peptide standards, correct?
A. The numbers that are produced are different.
Q. And the numbers are different because different standards are used, correct?
A. The numbers are different because different standards are used, yes.
Q. And the molecular weights in Sandoz's ANDA obtained using protein standards to calibrate the SEC column are higher than 10,000 kilodaltons, correct?
A. I believe the numbers that they reported are above 10,000 in most cases.
Q. And they're above 10,000 when the protein standards are used to calibrate the SEC column as opposed to the peptide standards, right?
A. They're above 10,000 when the protein standards are used, yes.
Q. But you didn't rely on those numbers, that is the molecular weights obtained using the protein standards, correct?
A. I did not rely on those.
Q. You ignored those, correct?
A. No, I did not. I considered them. I did consider them to be inappropriate standards so didn't rely on them.

Q. Now, the protein standards that were used for calibration in the Sandoz ANDA were commercially available when the patents were filed in 1994 and 1995, correct?
A. I don't remember specifically what they were.
Q. If we could look in your binder at Exhibit 3294.
A. 3294?
Q. Yes, sir.
A. I don't think I have it.
Q. Should be in there.
A. Which binder are you referring to?
THE COURT: Do you have Grant cross exam?
THE WITNESS: No, I do not. I have direct exam.
Q. Let me get you a binder. There you go.
A. Thank you.
Q. You're welcome.
A. Okay.
Q. And if we could take a look at the Bates number page ending with Bates number 2020, if we go to that page?
A. Okay.
Q. And this is in Sandoz's ANDA. This is a description in the middle section regarding the analytical methods using the protein standards to calibrate the SEC column as opposed to the peptide standards, correct?
A. That's what it says, yes.
Q. And on the screen we have the sentence highlighted, the

chromatograms are calibrated using commercially available protein standards?

THE COURT: Could you slow down just a little bit.

MR. ACKER: Yes.

THE COURT: Thanks.

THE WITNESS: Yes, that's what I read.

Q. And those protein standards were available in 1994 and 1995, correct?

A. Well, let's see. I'm familiar with these proteins, and I don't have catalog from that time, I would think that they probably were.

Q. So someone picking up the asserted patents in this case in 1994 and 1995 and seeing a reference to the SEC technique using the Superose column, would know that these protein standards were available, commercially available to calibrate that column, correct?

A. If they were in fact commercially available, a person skilled in the art would probably know that.

Q. But the peptide standards, that is the peptide standards that were used to calibrate the column to calibrate the molecular weight numbers that you relied on, those were not available in 1994 and 1995, correct?

A. If you mean by available that they weren't listed in a catalog, I believe that's correct.

Q. And, in fact, a patent application was filed in 1998 by

Alexander Gad, a scientist at Teva claiming he invented peptide standards to measure co-polymer-1, correct?

A. I, you know, I've looked briefly at the patent, but I haven't read it completely.

Q. Why don't look at your binder at exhibit 3539.

THE COURT: You're offering 3249 or is it --

MR. ACKER: Yes, your Honor, I would offer 32 --

THE COURT: Or is it 94? 94?

MR. ACKER: Yes, your Honor. 294?

THE COURT: Any objection?

MR. JAMES: No objection, your Honor.

THE COURT: Now, where are we going?

MR. ACKER: 3539, your Honor.

THE COURT: Thank you.

Q. Do you have that in front of you, Doctor?

A. Yes, I do.

Q. And this is the Gad patent that was filed in 1998 by, as inventor Alexander Gad, and you see just in the title of the patent it claims co-polymer-1 related polypeptides for use as molecular weight markers and for therapeutic use. You see that?

A. I do.

Q. And what is claimed in this patent is peptide standards to use as markers are standards to calibrate a column to measure co-polymer-1, right?

A. As I said, I haven't read the patent completely, so I'm not sure if that's all it's claimed.
Q. But you understand that is part of what is claimed, correct?
A. I really would have to review the patent before I could answer that.
Q. Well, were you aware of any peptide standards designed to measure co-polymer-1 that were available, and no one skilled in the art, before this patent was filed in 1998?
A. Again, if you're asking me if you mean by available if you could go to a catalog and purchase, then I'm not aware of that.
Q. Well, would it have been known to one skilled in the art before this patent was filed in 1998, to use these markers claimed in the patent to calibrate a column to measure co-polymer-1, using SEC?
A. I think a person skilled in the art could use polypeptide markers.
Q. So you think this patent was filed in 1998 was obvious?
MR. JAMES: Objection, your Honor.
THE COURT: Sustained.
Q. Well, but it's your opinion that one of skilled in the art would not use, would not have used protein standards to calibrate a column in 1994, is that right?
A. That's -- I think that those are not appropriate standards.
Q. And you think they're not appropriate standards because you

believe that the protein standards are different in their size and molecular weight relationship than co-polymer-1, is that right?

A. Yes.

Q. But it's true, isn't it, that Teva attempted to measure the molecular weight of co-polymer-1 in 1987 using protein standards to calibrate an SEC column, correct?

MR. JAMES: Your Honor, we limited our direct examination to infringement under the parties' agreement.

THE COURT: I assumed Dr. Grant, is he coming back?

MR. JAMES: Dr. Grant will -- he is on our list to come back during the rebuttal case, yes.

MR. ACKER: Your Honor, he's testified about six times that he believes one of skilled in the art would not have used proper --

THE COURT: I don't have a problem with this area.

Q. Yes.

THE COURT: I just wanted to make sure -- I guess I gathered Teva wants to make sure we're sticking to the division here. Go ahead.

MR. ACKER: Thank you, your Honor.

MR. JAMES: Thank you, your Honor.

Q. But it's true, isn't it, Doctor, that in 1987 when Teva first wanted to measure the molecular weight of co-polymer-1, it used protein standards to calibrate the SEC column?

A. I think they did.
Q. Why don't we take a look at document 3275, if you go to page three on 4991. Do you have that page in front of you, Doctor?
A. Yes, I do.
Q. And you see this is a Teva document, and it's dated March 8th, 1987. Do you see that? It's also up on the screen if you --
A. I see it.
Q. And handwritten notes, preliminary analytical studies on cop-1, you see that?
A. I see it.
Q. And then there's in section 2.5.1 there is a list of the proteins that were used to calibrate the SEC column in order to measure co-polymer-1, correct?
A. I see that.
Q. And those are protein standards, correct?
A. They are.
Q. Also true that in 1998 Teva hired a consultant, W. R. Grace to attempt to measure the molecular weight of co-polymer-1 and they also used protein standards to calibrate the SEC column to do so?
A. I don't recall that, but I think what you're referring to here was just a testament. It wasn't actually a calibration.
Q. Let's go back to that document and let's look at section

4.1 if we could.

And isn't it clear, Doctor, in section 4.1 where it says molecular weight calibration curve, that protein standards are being used to calibrate the column?

A. That's what it says. But I think it was later clarified that this was just a testament.

MR. ACKER: Your Honor, I move for admission, your Honor, of document 3275, DTX-3275.

THE COURT: Any objection?

MR. JAMES: No objection, your Honor.

THE COURT: It's admitted.

(Defendant's Exhibit DTX-3275 received in evidence)

Q. Why don't we take a look at table one. See that table, Doctor? You see there is a listing of the different batches down the left column, and then there's three rows of different molecular weights obtained using three different techniques, do you see that?

A. Yes, I do.

Q. And, for instance, for batch one using the protein standards that were commercially available, the resulting molecular weight was 58 kilodaltons, correct?

A. That's what it says.

Q. But when viscosity was used, which is a different direct method to measure molecular weight, the molecular weight obtained was 14,000 daltons, correct?

A. Let me just step back a minute. I don't see where it says that the protein standards were used there.
Q. Well, if you go back to what we just looked, at section 4.1, it describes the molecular weight calibration curve, correct?
A. Again, I don't think that was a calibration curve that was used for that purpose.
Q. Why don't we take a look, if you would, at page 304995. And I have it highlighted on the screen for you, Doctor.

In the middle of that paragraph it reads: It is well known that the molecular weight value obtained by gel filtration is related with the secondary and tertiary structure of polypeptide molecule. Cop-1 is a highly charged linear polymer, while markers using this study are globular proteins. You see that?
A. Yes, I do.
Q. So it's clear that what was used was commercially available proteins, right?
A. They used them for a very short period of time, but then they abandoned them.
Q. So in 1987 when the scientists at Teva first decided to try to measure co-polymer-1, they used globular proteins to calibrate the SEC column?
A. They used them for a short period of time.
Q. Would you consider the scientists at Teva that were doing

this work to be one of ordinary skill in the art?
A. I don't know. I didn't know the scientists.
Q. Now, going to Teva's consultant W. R. Grace, they also, in 1998, attempted to measure molecular weight of co-polymer-1 using commercially available protein standards, correct?
A. I don't recall that. Can you clarify it for me?
Q. Sure. Why don't you take a look at document 1762, please.
THE COURT: What was that number?
MR. ACKER: 1762, your Honor.
A. Okay, I have it.
Q. You see it's a memo from W. R. Grace to Teva to Mr. Barconi dated May 4th, 1988; you see that?
A. Yes, I do.
Q. And the first sentence it reads: Attached is a copy of our report entitled preliminary screening of cop-1 batches 13 and 11A. We have already begun to work on the use of alternative molecular weight calibration standards for size exclusion chromatography; you see that?
A. I do.
Q. And then if you go to page 360357, and you see the -- highlight the second bullet point, it reads: Calibration curves based on globular proteins yield cop-1 molecular weights four to six times higher than molecular weights calculated by ultracentrifugation or viscosity measurements; do you see that?
A. Yes, I do.

Q. So you would agree with me, wouldn't you, Doctor that in 1998, or excuse me, 1988 when W. R. Grace, Teva's consultant first attempted to measure the molecular weight of co-polymer-1, they used SEC calibrated with globular proteins?
A. I wouldn't interpret it that way.
Q. Despite what the words say?
A. Well that's what the words say, but that's not how I characterize it.
Q. If you take a look at page 360359. Are you there, Doctor?
A. 360359?
Q. Yes, sir.
A. In 1762?
Q. Yeah. There's two sets of Bates ranges, the larger Bates range.
A. Could you repeat that?
Q. Sure. 360359.
A. I don't have 360.
Q. There's -- you see there's two sets of Bates ranges there. You have to look at the one that's higher?
A. Oh, okay. 360359?
Q. Yes, sir.
A. Sorry. Okay.
Q. And it's on the screen for you. Draw your attention to the sentence that begins after the word second. This is what W. R. Grace is telling Teva 1988. Second, appropriate molecular

weight standards have not yet been found. Calibration with globular protein standards yields calculated molecular weights for cop-1 at least four to six times higher than molecular weights determined by viscosity and ultracentrifugation techniques. You see that?

A. I see that.

Q. So it's true, isn't it, that W. R. Grace in 1988, when they first attempted to measure co-polymer-1 using the SEC technique, calibrated their column using commercially available globular protein standard?

A. That's what this says.

(Continued on next page)

Q. And isn't it also true, sir, that in 1995 the Federal Drug Administration, the FDA suggested to Teva that they change their standards from a copolymer-1 self-standard and go back to a commercially available protein standard in order to use SEC to measure copolymer-1?

A. I think I recall they had that discussion.

Q. Why don't we take a look, if we could, at DTX1770. And if we could -- do you see that?

A. I have.

Q. Do you see there's an internal document at Teva referring to conversations with the FDA and it reads, dated April 9, 1995: "Dear Stan, attached please find the proposal we prepared for changing the method of calibration of the molecular weight distribution in Copaxone. Following our meeting with the FDA, they promised us a review of this proposal and comments on it." Do you see that?

A. I see that.

Q. Then if we go look at the next page there's a description of that meeting with the FDA. "Following meeting with FDA representatives on August 30, 1995, it was agreed to change the method of calibration for molecular weight determination. Presently the calibration methods use copolymer-1 markers and controls which were synthesized by Teva. These markers and controls have a wide range of molecular weight distribution and are not commercially available. The FDA chemist suggested that

we use commercially available proteins or peptides with well defined and narrow molecular weight for calibration. These calibrations can be performed in any analytical laboratory not relying on a single source for markers."

That's what the FDA told Teva in 1995, correct?

A. That's what it says there.

Q. And you would agree with me, wouldn't you, that the chemists at the FDA are ones skilled in the art?

A. I didn't know the chemists. I don't know that I could say that.

Q. Now, as you testified yesterday, even --

MR. KRAMER: Your Honor, I would move for admission of DTX1770.

MR. JAMES: No objection, your Honor.

THE COURT: Admitted.

(Defendant's Exhibit DTX 1770 received in evidence)

MR. ACKER: And I would move for the admission of the Grace memo DTX1762.

MR. JAMES: No objection, your Honor.

THE COURT: All right. Admitted.

(Defendant's Exhibit DTX 1762 received in evidence)

Q. Doctor, as you testified yesterday, even after you select what type of standard to use, you then must use another method or technique to determine the molecular weight of the standard, correct?

A. Yes.
Q. In other words, before you can calibrate an SEC column using a known standard you have to know the molecular weight of the standard, right?
A. They have to be determined, yes.
Q. Otherwise it wouldn't be a known standard, right?
A. Yes.
Q. And some of the methods you can use include viscometry, malls, mass spectrometry and ultracentrifugation, correct?
A. Correct.
Q. And you yourself are of the opinion that the way to do it, to measure the standards, is to use mass spectrometry, correct?
A. I don't completely agree with that.
Q. You testified during deposition on February 2, 2010, correct?
A. I don't remember the date, but --
Q. And there's a copy of the transcript in front of you.
MR. KRAMER: Counsel, I'm referring to page 72, line 23 to page 73, line 13.
MR. JAMES: Sorry, which date?
MR. ACKER: It's February 2, 2010, page 72, line 23. To 73, 13.
Q. And on that day while under oath you provided the following testimony, didn't you, Doctor?
(Video played)

MR. JAMES: Your Honor, I would just object. This is not inconsistent with the testimony.

MR. ACKER: It's going to be inconsistent right here.

THE COURT: All right, I've read it and I've heard it now. I could just finish it.

MR. ACKER: All right.

Q. Isn't it true, Doctor, that you believe that mass spectrometry is a technique that you would use to measure --

A. No, it's not true.

Q. So what technique would you use to measure standards?

A. I would use the techniques that were available.

Q. Your testimony today is you would use any standard and any standard would give you the same result?

A. I don't know what you mean by any standard.

Q. Well, would you use any standard besides mass spectrometry to measure the standards?

A. Your question doesn't make sense.

Q. Well, you have to use some technique to measure the standard, correct?

A. Yes.

Q. In your opinion, what technique would you use to measure standards, to measure copolymer-1 using SEC?

A. Any of the techniques that are available.

Q. And you think that any of the techniques available would be an appropriate technique to measure the standard?

A. I think they could be.
Q. Now, once a column is calibrated with a calibration curve the peak molecular weight corresponding to any elution volume or retention time of an actual sample can be determined by looking at the chromatogram and the calibration curve, right?
A. There's a lot in that question. Could you repeat it?
Q. Sure. Once a column is calibrated with a calibration curve the peak molecular weight corresponding to any elution volume or retention time of an actual sample can be determined by looking at the chromatogram and the calibration curve, correct?
A. That seems correct.
Q. And thus the resulting molecular weight attained for the sample to be measured when using the SEC method will be reflected by the standards used to calibrate the column, correct?
A. That's correct.
Q. So what standard you use to calibrate the column will determine what the resulting molecular weight is determined to be?
A. Yes. You should use appropriate standards.
Q. And when you use different methods to determine the molecular weight of copolymer-1 you get different values depending on which method is used, correct?
A. I disagree.
Q. But that was Teva's experience, correct?

A. I'm not sure I'm completely familiar with everything Teva did.

Q. Why don't we take a look at document 3137. Do you have that document, sir?

A. I do.

Q. If we could highlight the second paragraph, please?

THE COURT: Is there any objection to this document?

MR. JAMES: I don't believe so, your Honor.

THE COURT: Okay, it's admitted. Go ahead.

(Defendant's Exhibit DTX 3137 received in evidence)

Q. If we take a look at the second paragraph, Teva wrote on July 4, 1996, "The molecular weight copolymer-1 which is a heterogeneous mixture of polypeptides has been determined so far by techniques such as analytical ultracentrifugation, SEC chromatography with light scattering detection or with a calibrated SEC column."

And then they wrote, "Depending on the chosen analytical technique, the average molecular weight of copolymer-1, RS03494 varies between 4,700 and 11,000 daltons," correct?

A. That's what it says.

Q. And then if we -- so it was the case as of July 4 of 1996 inside Teva when they used different techniques to measure copolymer-1 they got different molecular weights, right?

A. I'm not familiar with what Teva did. I have not seen any

evidence in this case to suggest any difference.
Q. Why don't we go to the last page, the conclusion. Section 4.0, the conclusion, Teva sums up, "Molecular weights for copolymer-1 RS0394 determined by traditional analytical methods such as light scattering ultracentrifugation or SEC chromatography are in the range of 7000 to 11,000 daltons. The difference are due to the experimental bias in analytical technique and how data are calibrated and presented. Therefore, it should be explicitly stated by which analytical method the molecular weight data were obtained. Do you see that?
A. I see that.
Q. So you would agree with me that based on the documents as of July of 1996 inside Teva when they used different techniques to measure copolymer-1 they got different molecular weights, correct?
A. If that's what the documents say, that's what they say.
Q. And the recommendation was because of that you need to expressly state what technique is being used, correct?
A. That's what they said.
Q. It's also true that Teva got different readings, molecular readings when they used different techniques to measure their copolymer-1 self standards, correct?
A. I don't recall.
Q. Why don't we take a look at document 3509? And if you go

to --

THE COURT: I'm assuming that there's no objection to the use of these documents.

MR. JAMES: Not that particular document, your Honor.

THE COURT: Then it's admitted.

(Defendant's Exhibit DTX 3509 received in evidence)

Q. If you go to a table at 11166167, are you there, sir?

A. Yes, I am.

Q. And you see that the table reads average molecular weight of copolymer-1 markers obtained by three different methods; ultracentrifugation, viscometry and malls, correct?

A. That's correct.

Q. This is again the process by which Teva is attempting to determine the molecular weight of the markers or the standards to be used to calibrate an SEC column, correct?

A. It doesn't say that in the table.

Q. Well, it says average molecular weight of copolymer-1 markers on the top. Do you see that?

A. Yes, I see that.

Q. So these are a bunch of different markers and there's actually a heading there for the markers, correct, on the left side?

A. Correct.

Q. And then the top across there's three different methods being used to measure those markers, right?

A. Right.
Q. And we take a look, for example, at the first marker, when ultracentrifugation was used there was a reading of 6,000 daltons, right?
A. That's what it says.
Q. And when viscometry was used there was a reading of 7500 daltons, correct?
A. That's correct.
Q. So there is a difference of 1500 daltons with two different methods used, right?
A. There is a difference of 1500 in those two numbers.
Q. If we go down to the marker 50695, you see when ultracentrifugation was used, no, one up, 50695. When ultracentrifugation was used to measure the marker there was a reading of 7200 daltons, right?
A. I see that.
Q. But there was a reading 1500 daltons higher when malls was used, correct?
A. 8700 and 7200. Those numbers are different by 1500, yes.
Q. And then if we could go down to BD422, again, here we have a situation where when ultracentrifugation was used, there was a reading of 13,800 daltons, right?
A. That's what it says.
Q. But when malls was used, there was a reading of 2,000 daltons higher, correct?

A. 13,800 to 15,800, that's 2,000, yes.
Q. And this was the experience inside of Teva, correct?
A. They put this table together. I assume so.
Q. Now, in the asserted patents, although it does make a reference to using SEC and Superose column there is no mention of what standards are to be used, correct?
A. That's correct, but I don't think that makes a difference.
Q. And there's also no mention of what method should be used to measure the standards, correct?
A. That's correct.
Q. And you would agree with me, wouldn't you, Doctor, that the use of self-standards with SEC only provides calculated molecular weight averages that are at best an approximation relative to the standard used?
MR. JAMES: Your Honor, I would object. As we discussed earlier, we limited our direct examination to issues of infringement. This clearly is going to the issue of indefiniteness and invalidity.
THE COURT: It sounds that way to me.
MR. ACKER: Your Honor, it's a direct response to his repeated testimony that no one would use protein standards and everyone would know how to do it, you get the same molecular weights however you did it.
MR. JAMES: That was his testimony on cross-examination, your Honor.

MR. ACKER: That was his testimony yesterday and today.

THE COURT: This is all about invalidity. I suppose it also goes to impeachment. Do you not want a preview?

MR. JAMES: I'd love a preview, your Honor, I'm trying to figure out what the rules are here. We thought --

THE COURT: I understand. They're not working.

MR. ACKER: I'll move on. I'm almost done with this area. I have two more questions.

THE COURT: Okay, all right.

MR. JAMES: Thank you, your Honor.

Q. Doctor, again let me repeat the question. You would agree with me that the use of self-standards with SEC only provides calculated molecular weight averages that are at best an approximation relative to the standard used?

A. No, I don't agree.

Q. Why don't we take a look at DTX3509? If you would go to page 1116165.

A. Could you repeat that number?

Q. Sure. 1116165.

A. Okay.

Q. And we have it on the screen for you if it's easier and this again is that same Teva document, and what Teva wrote was, "The calibration curve for a given system is obtained by injecting a series of standard samples of known average

molecular weights. However, for the curve to be valid the calibration standards used should have the same conformation and chemical structure as the sample to be analyzed. As a result, the sample molecular weight distribution and the calculated molecular weight average are at best an approximation relative to the standard used."

Do you see that?

A. I see it.

Q. And do you agree with that sentence, that as a result the sample molecular weight distribution and the calculated molecular weight average are at best an approximation relative to the standard used?

A. No, I don't agree.

Q. Let me turn now to your testimony regarding the species claims, infringement of the species claims. Do you understand what I'm referring to when I refer to the species claims?

A. You're talking about percent on mole fraction?

Q. Yes. Now, the molecular weight measurements you relied on to reach your opinion on these species claims also came from Sandoz' ANDA and they were calibrated by using SEC with peptide standards being the calibrant, correct?

A. Yes.

Q. And what resulted from the SEC was a chromatogram, right?

A. Yes.

Q. And then you used, and I'm going to refer to it as the

slice method, to determine whether or not there was a transmitter?

A. Correct.

Q. And if we could put up slide 31 from your PowerPoint, this is the slice that you used it's a depiction, representation of the slice method you used?

A. It's an illustration of the slice method that was used by Sandoz.

Q. But one core assumption underlying the slice method is that each slice, each one of the slices that we're looking at is narrow enough so that each slice is attributed to a singular molecular weight value, right?

A. That was the case with the data that was provided.

THE COURT: I'm sorry, I didn't hear that.

THE WITNESS: That was the case with the data that was provided.

Q. But isn't it true that each slice does not contain only molecules of a singular molecular weight?

A. If you mean by a singular molecular weight a single molecule, one distinct molecular weight, then each slice probably does not.

Q. Isn't it true that you have no idea how many different molecular weight species are in each slice?

A. Probably not exactly.

Q. No way for you to tell exactly how many different species

of different molecular weights are in each slice, correct?
A. How many different species of each molecular weight -- could you repeat that?
Q. Isn't it true that you have no idea how many different molecular weight species are in each slice?
A. No, that's not true.
Q. Did you do a calculation to determine how many exact species of different molecular weights are in each slice?
A. I did a calculation. I didn't do a calculation, Sandoz did a calculation.
Q. Isn't it true that each slice, even when you attribute only one molecular weight to that slice, there are molecules that have many different molecular weights in that slice?
A. I'm not sure what you mean by many different.
Q. Well, there's, all of the molecules don't have the same molecular weight in that slice, right?
A. That slice, if it's very narrow, they have very similar molecular weights.
Q. But they're different than the molecular weight that you've attributed to the slice, correct?
A. Not necessarily.
Q. Some will have different molecular weights than what you've attributed to the slice, right?
A. Some might.
Q. And you have no idea knowing how many will have molecular

weights that are different than the molecular weight that you attributed to the slice, correct?
A. I don't think that's necessary.
Q. But the answer to my question is you don't know how many of the molecules in that slice have a different molecular weight than what you've attributed to the slice, correct?
A. I didn't calculate how many molecules.
Q. So you don't know how many molecules have different molecular weights than the molecular weight you've attributed to the slice, correct?
A. I think you could analyze it to probably get that answer, but I didn't do that.
Q. And so the molecular weights for each slice represent only an average molecular weight, average molecular weight of all the individual molecules present in the slice, right?
A. Yes, but that's sufficient.
Q. And thus the slice analysis provides only an estimation of the total amount of each copolymer-1 sample within the claimed molecular weight ranges, correct?
A. It gives you a value that's very representative.
Q. But it's an estimate, right?
A. It's not an estimate. It's a value that's determined from the calibration.
Q. It's an approximation, isn't it?
THE COURT: All right, I don't think we need to go any

further on that.

MR. ACKER: All right. That's all I have. Thank you.

THE COURT: Okay.

MS. BLOODWORTH: Your Honor, would you like to take a break? I have a couple of questions to ask Dr. Grant.

THE COURT: Fine, take a ten-minute break.

(Recess)

THE COURT: Go ahead, Ms. Bloodworth.

MS. BLOODWORTH: Thank you, your Honor.

CROSS-EXAMINATION

BY MS. BLOODWORTH:

Q. Dr. Grant, if you can get your direct binder, we'll use some of the exhibits on that one as well.

A. Okay.

Q. Thank you. Now, Dr. Grant, you testified during your direct that once an SEC column is calibrated you can calculate the average molecular weight of any sample from that calibration, correct?

A. Any sample that falls within the range of the calibration.

Q. Okay. So to be appropriately calibrated the sample needs to fall within the range of the calibration.

A. Calibration has to be done for the range of the column.

Q. Okay. And you also testified that you've used for the Mylan infringement analysis SEC data provided by Mylan, is that correct?

A. That's correct.
Q. And if we could call up slide 32 from your direct. And to calculate the molar fraction limitations, if I refer to the 2 to 20 and greater than 40, 5 percent 2-1/2 percent over 40 as to the molar fraction limitations, is that clear to you, Dr. Grant? For the claims I'm going to ask you about, I'm going to call them the molar fraction claims, and those are the ones that cover the 2 to 20 and the more than 5 percent, more than 2-1/2 percent over 40?
A. Yes.
Q. So to calculate the molar fraction claims this is the equation that you used, correct?
A. That's correct.
Q. It requires having on the denominator of the calculation the total number of molecules across the range of the distribution, correct?
A. It requires having the calculation of the total number of molecules in that range, yes.
Q. Okay. And do you recall the approximate range for the distribution of the Mylan lots that you calculated?
A. Which range are you referring to?
Q. The range of the distribution of the copolymer-1 samples, the GMA 001/009 for the molar fraction claims.
A. The molecular weight range?
Q. Yes.

A. Don't recall exactly what the whole range was, but it was a range that was supplied by Mylan.
Q. If you could please put up slide 46. And this is just to refresh your recollection to reorient you, Dr. Grant. This is the ranges, this is the percentages that you calculated for the GMA lots 001, 002 and 003-09, correct?
A. Correct.
Q. If you could turn in your binder, your cross-examination binder that I just handed you, to DTX 2029.
A. Okay.
Q. You can see at the top of the page it says MW and then MYL 0001050.
A. I see that.
Q. And right below that it says GMA 001/009. Do you see that?
A. Yes.
Q. If you could turn to the next page, please? And in the third column, the heading is sum 2302 percent between 2000 and 20,000 is 83.13 percent. Do you see that?
A. Yes. That's what it says.
Q. And that's the same value that you calculated or reported on slide 46 for that lot, right?
A. I don't remember the slides.
Q. 83.13 in front of you and we'll show slide 46 again.
A. Yes, the 83.13. Greater than or equal to.
Q. Greater than or equal to, fair enough. Now, still looking

at DTX 2029, this is the data that you calculated your percent molar fraction from for GMA 001/009 correct?

A. It looks as though it is.

MS. BLOODWORTH: I move DTX 2029 into evidence, your Honor.

MR. JAMES: No objection.

THE COURT: All right, admitted.

(Defendant's Exhibit DTX 2033 received in evidence)

Q. And if you could turn to the next tab in your binder, Dr. Grant. It's marked DTX 2033.

A. Okay.

Q. And at the top of this page it reads MW and then MYL 0001068. Do you see that?

A. Yes, I do.

Q. And underneath that it says GMA 002/009. Do you see that?

A. Yes.

Q. Turn to the next page, please? The third column, the heading is sum 2358 percent between 2000 and 20,000 is 81.7 percent. Do you see that?

A. I do.

Q. Thank you. Leave that page in front of you. Could you put up slide 46 again? And that's the same value that you reported for GMA lot 002-09, correct?

A. I reported greater than or equal to 81.70 percent.

Q. Greater than or equal to. And the data in DTX 2033, you

recognize as the data you relied upon to calculate that value, right?

A. It looks like that, yes.

MS. BLOODWORTH: I move DTX 2033 into evidence, your Honor.

MR. JAMES: No objection, your Honor.

THE COURT: Admitted.

(Defendant's Exhibit DTX 2033 received in evidence)

Q. If you could please turn, Dr. Grant, to the next tab in your binder. And that's DTX 2037.

A. Okay.

Q. And the first page, again, says MW and then followed by MYL 0001079.

A. Yes.

Q. And underneath that it says GMA 003-09?

A. Yes, it does.

Q. Could you turn the page, please? In the third column, the heading is sum 2338 percent between 2000 and 20,000 is 89.5 percent. Do you see that?

A. I see that.

Q. And that's the value that you reported on slide 46, correct?

A. Greater than or equal to 80.95 percent, yes.

MS. BLOODWORTH: Your Honor, I move DTX 2037 into evidence.

MR. JAMES: No objection.

THE COURT: Admitted.

(Defendant's Exhibit 2037 received in evidence)

Q. Now, Dr. Grant, if you could please turn back to me, to the first tab in your binder, DTX 2029. And turning to the second page. The column all the way to the left has a number sign followed by a 1 and then it says slice RT and slice MW. Do you see that?

A. Yes.

Q. And the first row reports slice retention time -- RT stands for retention time, correct, Dr. Grant?

A. Yes, it does.

Q. The first row reports slice retention time of 19.617 and a slice molecular weight -- MW stands for molecular weight, right, Dr. Grant?

A. Yes.

Q. Slice molecular weight of 57,837, correct?

A. That's what it says.

Q. So that's the largest value in the molecular weight distribution for this lot, correct?

A. That's the largest value that was reported.

Q. That was reported. And if you turn to the last page of the exhibit, please. It has a page number 32 on the bottom.

A. Okay.

Q. And if you look at the second to last row, it's number

1081, and it has a retention time reported of 37.617, correct?
A. Yes.
Q. And the slice molecular weight for that is 497, correct?
A. That's what it says.
Q. So this copolymer-1 data that you used to calculate the distribution ranges from 497 to 57,837, correct?
A. Actually goes from 494.
Q. 494?
A. To 57837.
Q. Excuse me, so 494 to 57,000, 58,000, approximately. And a similar large range will be found in the lot for GMA 002/009, correct, if you turn to DTX 2033?
A. There's a large range there that's similar but not the same.
Q. That range is from 64,047 to 484?
A. That's right.
Q. And for the third lot under DTX 2037, a similar range, this time from 60,034 down until 374, correct?
A. That's right.
Q. So upwards of approximately 60,000 daltons?
A. You mean the range?
Q. The range.
A. Approximately.
Q. And during your direct I believe you testified that the calibration markers that Natco relied upon were peptide,

polypeptide markers, correct?
A. Yes.
Q. If you could get your direct exam binder please, sir? And if you could turn in that binder to PTX 318.
A. Okay.
Q. And if you could look at the page ending in 112.
A. I have it.
Q. And I believe you testified about the first paragraph on this page in your direct testimony. Do you recall that?
A. Yes.
Q. And what you didn't do was go down and look at the actual standards and the molecular weights for the standards that Natco uses, correct?
A. No, that's not correct.
Q. You didn't do it in your direct testimony?
A. I don't think I was asked to.
Q. Okay. Well, let's look at it now. So there are six standards that were used to generate the SEC data you relied upon?
A. Yes.
Q. And the molecular weight for those standards range from 3,757 daltons to 9,220 daltons, correct?
A. That's correct.
Q. So the area that's calibrated is from 3,757 to 9,220.
A. No, that's not correct.

Q. Did you receive calibration data from Natco to do your calculations?
A. The data that I received from Natco already had the molecular weights calculated.
Q. Did you look at the calibration curve that was provided to you with that data?
A. I looked at the calibration curve that was associated with that data, yes.
Q. And the calibration curve was based on these markers, correct?
A. I believe that's true.
Q. And these markers calibrate a range from 3,757 to 9,220, correct?
A. They span that range.
Q. Have you ever seen any Natco calibration markers that are greater than 9,220?
A. I don't believe that I have.
Q. You didn't review any for your direct testimony, correct?
A. I don't recall.
Q. Your direct testimony?
A. Oh. No, I did not.
Q. I understand you submitted quite a few expert reports, but this is the only one that had SEC data in it, correct?
A. Could you repeat the question?
Q. Sure. This is the only -- this data that you've relied

upon, this is the only, you only submitted one expert report that relied upon SEC data, correct?
A. I relied upon data that was supplied to me by Mylan.
Q. And you looked at the calibration markers, correct?
A. Yes, I did.
Q. And you did not find any data for any calibration markers greater than 9,220?
A. No. It wasn't necessary.
Q. How did you calibrate the column for the range from 10,000 to 60,000?
A. I didn't calibrate the column.
Q. Who did?
A. Mylan did.
Q. What do you have to rely on that?
A. Calibration curve that I see in association with these same lot numbers.
Q. Okay. Well, let's look at -- you can turn in your direct binder still to PTX 325.
A. Okay.
Q. And if you could turn to the page ending in the Bates range 1057.
A. Okay.
Q. And there's a box underneath the graph and that lists the calibration markers. Those are the same values that we were just looking at, correct, the 3757 to 9220?

A. I didn't memorize them. I'm not sure they're the same.
Q. Do you want another page reference that you can double check?
A. Sure.
Q. Could you turn back to PTX 3138 and the page ending 1112? Excuse me, 112.
A. Yes, the same molecular weights are listed there.
Q. Just to make sure the record is clear, we're now looking at PTX 325 with the page ending in 1057 and this also lists the retention times for those molecular weights, correct?
A. Yes.
Q. Then there's a graph above it?
A. Yes.
Q. And that's the calibration curve, correct?
A. That's correct.
Q. And that's the calibration curve that you relied upon that you were referring to in your answer previously?
A. No, that's the calibration curve that Mylan relied on.
Q. Mylan relied on that calibration curve?
A. They did the calculations of the molecular weight.
Q. Okay. Of the peak molecular weight, correct?
A. No, they did the calculations for all the slice molecular weights in the data they supplied.
Q. Let's look at right there on the graph, all those boxes, each little box represents a calibration marker, correct?

A. Yes, it does.
Q. Are there any boxes higher than 26.466 on the retention time?
A. No, they're not, but they don't have to be.
Q. And there are none below 3664, correct?
A. That's correct.
Q. So this calibration, these markers cover about a 10 percent range of the 60,000 range that's in the entirety of the distribution, correct?
A. If you mean the -- well, I'm not sure about the 60 percent, but they cover a range within the calibration.
Q. There's no marker that's used at 20,000 daltons, correct?
A. No, but the way this curve is done it's not necessary.
Q. And there's no marker at 15,000 daltons, correct?
A. The way this curve's done it's not necessary.
Q. And there's nothing at 2,000 daltons, correct?
A. I don't see anything there.
Q. So let's look at what this curve has done. Could you please go back down for me into your cross-examination binder? And you'll see in the first tab the DTX, that's defendant's TX 2029.
A. Okay.
Q. Okay? At the very top it says MW, MYL 0001050. Do you see that?
A. I do.

Q. If you could please turn in your direct binder back to P as in Paul TX 325?
A. Okay.
Q. And turn to page ending or turn to page MYL 0001050?
A. Okay.
Q. And in section 7 it states that the molecular weight distribution by SEC, and I believe you relied upon this in your direct testimony, supports a result of .335, correct?
A. That's what it says.
Q. It says for the specification between 5,000 and 9,000 daltons. Do you see that?
A. I see it.
Q. There was no reliance in reporting in using this data to make this certificate of analysis on anything at 20,000 daltons, was there, sir?
A. I didn't understand the question.
Q. In the specification of the certificate of analysis on page MYL 0001050, is there any reported value outside 5,000 to 9,000?
A. It says between 5,000 and 9,000.
Q. Between 5,000 and 9,000.
A. For peak molecular weight.
Q. For peak molecular weight. There's no value reported at 20,000, is there, sir?
A. I don't see one.

Q. And there's no value reported of a percent distribution between 2 and 20, is there?
A. No, there is not.
Q. And the data calculated DTX 2029 that you relied upon is the data underlying this certificate of analysis, correct?
A. I believe it is.
Q. And then let's turn, still at PTX 325, looking at page ending in 1068, and could you please show DTX 2033? What I have up on the screen for you, Dr. Grant, is DTX 2033 and that has a page number at the top MYL 0001068. Do you see that?
A. I see it.
Q. And you also have in front of you PTX 325 that has a certificate of analysis reported on MYL 1068, correct?
A. Yes.
Q. And again for part 7, it has a molecular weight distribution by SEC reported of 6431 and the specification is between 5,000 and 9,000 daltons, correct?
A. That's what it says, but that's not a distribution.
Q. Okay. And let's go to the next one. That's not a -- I'm sorry, sir? Excuse me? That's not a distribution?
A. It's not a distribution. It's just a peak molecular weight.
Q. What's reported here is just a peak molecular weight. There's no distribution reported with the data associated with it from 2033, correct?

A. I was talking about 1068.
Q. Okay. And the data that you relied upon underlying the calculation of the peak molecular weight wasn't used to report the distribution, correct?
A. I was supplied with data from Mylan that gave me, that reported the molecular distribution of their sample. They did the calculations of molecular weight.
Q. Maybe there's some confusion. Mylan provided you SEC data that was provided to you from Teva's counsel, correct? So you got your data from Teva's counsel.
A. Mylan -- yes, provided it to Teva's counsel and they provided it to me.
Q. And did Teva's counsel tell you that Natco was using that data to produce the distribution curve?
A. The data was a distribution curve.
Q. It was never used for that purpose, correct?
A. I don't know how it was used.
Q. Well, it was certainly calibrated in the area between 5 and 9,000 daltons, you agree with that, right?
A. It was.
Q. Let's turn to DTX 2037 now and stay with PTX 325 with me, sir, actually, we'll have put up 2037 and again looking at the top of that that is MYL 0001079. So if you could turn to PTX 325 to 1079, that's another certificate of analysis, this time for lot GMA 0309 and this in line 7 states molecular weight

distribution by SEC, the results are 6718 and the specification is between 5,000 and 9,000 daltons, correct?

A. For peak molecular weight.

Q. For the peak molecular weight. And we can also agree, correct, that the range of 5,000 to 9,000 is narrower than the calibrated markers that you relied upon, correct?

A. As a matter of numbers, those numbers are narrower than the distribution in the data that was provided to me.

MS. BLOODWORTH: Just one moment.

(Pause)

MS. BLOODWORTH: I found it, thank you.

Q. If you could stay in PTX 325 and look at the Bates number ending in 1057?

A. Okay.

Q. And so ending in 1057, looking at the chart in the middle. We can agree, can't we, Dr. Grant, that if the calibration curve changes, that your calculation numbers would change, correct?

A. I'm not sure what you mean.

(Continued next page)

Q. If the slope of your calibration line changes, your reported calculations that you relied that -- the data that you relied upon in underlying your calculations would also change, correct?
A. I'm still not sure what you mean by slope changing.
Q. If the line is not the same?
A. If the line's not the same, okay.
Q. If your calibration curve changes, it's altered, that alters your results, correct?
A. Well, if the correlation between retention time and molecular weight is different, it would be different, yes.
Q. And you submitted your last infringement expert report in the Mylan case on May 31st, 2011, correct?
A. I don't remember the date.
Q. Was this around May, June 2011?
A. I'm not sure. I just don't remember the date.
Q. I can show it to you.
A. Okay.
MS. BLOODWORTH: If I may approach the witness, your Honor?
THE COURT: You may.
Q. Just to refresh your memory, Dr. Grant, I hand you your supplemental expert report in this case, and -- excuse me -- your supplemental reply report in this case, and its dated May 31st, 2011, correct?

A. Yes it is.
Q. Okay, thank you.
MS. BLOODWORTH: Your Honor, I have no further questions. Thank you, Dr. Grant.
THE COURT: All right.
MS. BLOODWORTH: Approach again to get my book back?
THE COURT: Redirect?
MR. JAMES: I just have a little redirect, your Honor.
THE COURT: Okay.
REDIRECT EXAMINATION
BY MR. JAMES:
Q. Could we pull up trial exhibit 25, page 1057, please?
Dr. Grant, do you have that in your binder?
A. What page was it again?
Q. Yes, it's page 1057?
A. Yes.
Q. Counsel asked you some questions about the calibration that Natco performed on its products?
A. Yes.
Q. And, Dr. Grant, could you explain to the Court what is shown in that graph GPCV calibration plot?
A. That graph shows a calibration based upon a set of standards, and it shows it by retention time on the X axis -- Having retention time on the X axis, and the log of the molecular weight on the Y axis, and then it fits that data to a

straight line.
Q. And do the ends of that calibration curve plotted by Natco, are they -- do they extend beyond 2,000 and 20,000 kilodaltons?
A. Yes, I believe they do.
Q. And Dr. Grant, can you explain to the Court, is it appropriate to extrapolate the calibration curve beyond the range of the standards that you're using?
A. If the calibration is fit to a straight line, that can be done appropriately, yes.
Q. And, Dr. Grant, the data you were provided, did Natco and Mylan, did they associate the molecular weights with the retention times for the data you were provided?
A. Yes, they did.
Q. And for the calculations that you did for the percent between two and 20, you believe the calibration was appropriate?
A. I do.
Q. Dr. Grant, do you -- are you aware of any information supplied by Natco and Mylan where they relied on the calibration being appropriate between 2,000 and 20,000 daltons?
A. Yes, I am aware of that. In fact --
Q. Look at the next page.
A. It's on the next page, yes. Yes, on the next page, page 1058, they report results from this calibration curve for a percentage greater than 2,000 and percentage less than 20,000.

Q. Let's pull that up at the bottom of that page, underneath, right there. That would be fine. And you're talking about the little box at the bottom, Dr. Grant?
A. Yes, I am.
Q. Could you explain what's shown there to the Court?
A. Well, what is shown there is the result of an analysis of their, the molecular weight distribution of their sample based upon this calibration curve where they calculated the amount of material that was greater than 2,000. So they went to a 2,000 molecular weight retention time, and the material that was less than 20,000, so they went to a 20,000 molecular weight retention time.
Q. And is that the same thing that you did in your calculations, Dr. Grant?
A. Yes, it is.
Q. And, Dr. Grant, were these data provided by Mylan and Natco to the FDA?
A. Yes, these data were provided to the FDA.
Q. And Dr. Grant, are you aware of Mylan and Natco providing to the FDA number average and weight average data calculated from these same results?
A. Yes, they did.
Q. And in order to do that, do you have to extrapolate the curve across entire distribution?
A. Yes, you do. You have to extrapolate the curve from the

beginning of the chromatogram to the end of the chromatogram in order to get a calculation for number average and weight average molecular weight.

Q. And Mylan and Natco provided those data to the FDA as well?

A. Yes, they did.

Q. Dr. Grant, could you turn in the white binder that Mr. Acker gave you to DTX-3275?

A. Okay.

Q. And I believe counsel directed you to page 304994 and 304995 and I'd like to point out or take you to page 995, please.

A. Okay.

Q. And just a few lines down from the top, it says that -- well, let's start with the line where it says it is well known if you could highlight that sentence.

Dr. Grant, could you read that sentence and the next sentence into the record, please?

A. It says, it is well known that the molecular weight value obtained by gel filtration is related with the secondary and tertiary structure of polypeptide molecule. Cop-1 is a highly charged linear polymer, while the markers used in this study are globular proteins.

Q. Dr. Grant, what does that convey to you about the authors, what they were writing about that the similarity or differences between co-polymer-1 and protein standards?

A. Well, it tells me that the authors knew full well that the globular proteins that they were using didn't conform to the same size to molecular weight relationship that the sample did.
Q. And what's the date of this document, Dr. Grant? If you look in the upper --
A. 1987.
Q. That's August the 3rd, 1987?
A. Yes.
Q. Dr. Grant, have you reviewed this document previously?
A. I have.
Q. And are you aware of whether or not in this document Teva describes the use of self standards?
A. Yes, they do.
Q. Could you turn to page 304998?
A. Okay.
Q. Mr. Acker asked you some questions about table one?
A. Yes.
Q. Right?
A. Uh-huh.
Q. And let's turn over to page 305000. The title of that section is statistical analysis of the correlation between molecular weight determined by viscosimetry and retention time of the main peak on Superose 12 for cop-1; you see that?
A. Yes, I do.
Q. And, Dr. Grant, could you explain to the Court what is

provided on that page?
A. What is provided on this page is a list of cop-1 batch numbers 1, 3, 5, 7, 8, 9, 9A, 9B and ten and 11, as well as their molecular weights, and then it gives a measured retention time, as well as a calculated retention time.
Q. Okay. And what is viscosimetry?
A. Viscosimetry is the same as viscometry. It's another method used for calculating molecular weight or determining molecular weight.
Q. So do you understand this page to be providing data of co-polymer-1 batches measured by viscometry?
A. Yes, I do.
Q. And these co-polymer-1 batches, are these self standards?
A. Yes, they are.
Q. Could you explain to the Court why you believe that to be true?
A. Because I know that they started naming their self standards cop-1.
Q. And what makes them self standards?
A. They're self standards because they are basically the same material as co-polymer-1.
Q. And looking back at the page, the previous page, Dr. Grant, at figure three. At figure three, there is a line drawn on that graph. And if you could look at the title -- could you read the title into the record, Dr. Grant?

A. Yes. The title is, relation between molecular weight determined by viscosimetry and retention time of the main peak on Superose 12.
Q. What information is provided on this graph, Dr. Grant?
A. This graph provides calibration of retention time versus molecular weight based --
Q. I'm sorry, I didn't mean to interrupt you.
A. Based on viscosimetry.
Q. And what are the standards that are being used for this calibration?
A. These are cop-1 self standards.
Q. Let's look now at defendant's trial exhibit 7 -- 1762. Do you have that? It's also in the white binder.
A. Okay.
Q. And I believe that counsel directed you to page TEV3017833.
A. Okay, I have it.
Q. And in that second bullet point on that page, Dr. Grant -- perhaps it's easiest if could you just read the first two sentences of that bullet into the record, please?
A. It says, calibration curves based on globular proteins yield cop-1 molecular weights four to six times higher than molecular weights calculated by ultracentrifugation or viscosity measurements. This is consistent with cop-1 existing in solution principally as a random coil with few distinct structural features.

Q. Dr. Grant, what does that suggest to you about the author's understanding about the appropriateness of protein standards for measuring molecular weight of co-polymer-1?
A. That says to me that the authors knew full well that those were not appropriate standards for co-polymer-1.
Q. And in that second sentence you read it refers to a random coil, with few distinct structural features; what is that?
A. Random coil is just a name that scientists give to a polypeptide that does not assume a stable density back structure.
Q. And, Dr. Grant, if you could look back at page 3017831, what is the date of this report?
A. April 6, 1988.
Q. Dr. Grant, could you turn -- well, let me ask you a question before we go to the next exhibit. You've reviewed Teva's NDA, is that right?
A. I've seen portions of it.
Q. Okay. And you understand that the FDA approved Copaxone with its molecular weight being measured with co-polymer-1 self standards, correct?
A. Yes, they did.
Q. Let's turn now to DTX-3137. And if you look at the first page, Dr. Grant. I believe counsel pointed you to the second full paragraph in the introduction. Do you recall that?
A. Yes, I do.

Q. The first sentence says, the molecular weight for co-polymer-1, which is heterogenous mixture of polypeptides, has been determined so far by different techniques, such as analytical ultracentrifugation SEC chromatography with light scattering detection or with calibrated SEC column.

Dr. Grant, are all of those techniques the use of an appropriately calibrated suitable gel filtration column?

A. No, they're not.

Q. If you look at the last page, I'm sorry, page 290820. Counsel directed you to the first full paragraph, the last sentence. It says: Therefore, it should be explicitly stated which, by which analytical method the molecular weight data were obtained. Do you see that?

A. I do.

Q. Do the patents in suit explicitly state which analytical methods is to be used to determine the molecular weight?

A. Yes, they do. They explicitly state that you should use size exclusion chromatography.

Q. Now let's look at defendant's trial Exhibit 3509, Dr. Grant.

A. Okay.

Q. Counsel directed your attention to a table that appears on 1116167.

A. Yes.

Q. Dr. Grant -- if you could blow that up, please.

Dr. Grant, in that table there are data provided for ultracentrifugation, viscometry and something called MALLS for several different co-polymer-1 batches; right?

A. That's right.

Q. Maybe just for the Court's information could you explain what MALLS is?

A. MALLS stands for multi angle laser light scattering. It's just another way of determining molecular weight.

Q. And counsel pointed out to you that you get different values when you use these different kind of molecular weight determination techniques, right?

A. Well, they got different numbers.

Q. Dr. Grant, in 1994, was it well known how to appropriately apply these different values to get an appropriate calibration curve?

A. Yes, it was.

Q. And, Dr. Grant, have you graphed these different molecular weight values to determine whether you get a different calibration curve?

A. Yes, I did that.

MR. JAMES: Your Honor, permission -- I'd like to hand up an exhibit?

THE COURT: All right.

MR. JAMES: This will be plaintiff's trial exhibit 756.

Q. Dr. Grant, can you identify plaintiff's trial exhibit 756?
A. Yes, I can. This is a copy of the plot that I made of the numbers that were on the table that was on the previous slide that we just looked at.
Q. Those were the data that we were looking at in DTX-3509?
A. Yes, on page 6167.
Q. And, Dr. Grant, could you explain what you did when you plotted these data?
A. Yes. I took the data for viscosimetry ultracentrifugation analysis and MALLS analysis, and I assigned a retention time based upon the viscosimetry data, and plotted that retention time against the molecular weights that were in all three of the columns.

Once that plot was done, the different points that you see up there, the dots, the squares and the triangles, were fit by linear regression analysis to a straight line. And although it looks there is only one line there, all three lines are in fact there; dotted line for the MALLS, solid line for the ultracentrifuge and a dot dash line for the viscosimetry. And what this shows is that line is the same for all of them. So the molecular weight you determine for any of those would be the same.
Q. So, Dr. Grant, you're saying that on that plot shown on the screen, there are actually three calibration curves?
A. That is correct.

Q. And if you were to measure the molecular weight of a co-polymer-1 sample using any one of those three calibration curves, would the value obtained be different in any significant way?

A. No, it would not.

Q. John, could you pull up the slide that we used with the little slices shown chromatogram, thank you.

This is slide 31. Determination of molar fractions. Now, counsel asked you some questions about whether or not it was necessary to know how many different kinds of molecules were in each slice, and you said that it wasn't necessary. Do you recall that?

A. That's right, that's correct.

Q. Can you explain why you don't believe it's necessary to know how many different kinds of molecules or different molecular weights there are in those slices?

A. Well, that's because of what size exclusion chromotography tells you and allows you to do. It's really the only type of analysis method that will give us this molecular weight distribution.

And we're talking about, you know, determining the molecular weights of different slices. And you can take slices that are very very thin to reduce distribution of molecular weights in those slices, but it's perfectly acceptable to assign a single molecular weight to each slice as long as you

assign it at the same place along the slice.
Q. And is size exclusion chromatography, is it used to make these sorts of determinations in the literature, Dr. Grant?
A. Yes. Many many scientists over many many years have relied on this technique to do exactly that.
Q. And do you believe it's valid for this purpose?
A. I believe it's absolutely valid, yes.
Q. And do you believe the data that you were provided by Mylan and by Sandoz were valid for making these determinations?
A. Yes, I do.
MR. JAMES: I have no further questions.
THE COURT: All right. Anything further?
MR. ACKER: Four questions your Honor.
THE COURT: Four, okay.
MR. ACKER: I'm going to ask them here.
THE COURT: Okay.
RECROSS EXAMINATION
BY MR. ACKER:
Q. Dr. Grant, do the patents-in-suit state what standards should be used to calibrate the SEC column?
A. No, they don't.
Q. Do the patents-in-suit state what technique Teva used to measure the standards that it used to calibrate the SEC column?
A. No.
MR. ACKER: Two questions, your Honor. I'm done.

Thank you.

THE COURT: All right. Thank you very much, Dr. Grant. You may step down.

(Witness excused)

THE COURT: Next witness.

MR. WIESEN: Just a housekeeping matter before we call the next witness. We were able to get a stipulation from the defendants on one element that's contained in one of the patents. I have the stipulations here. Before we put the next witness on, we'd like to have them entered. We've actually done stipulations in order. I don't know if you prefer to do it that way or if we can just rework them and we can do them as stipulations and enter them as exhibits, however you prefer to do it, but I just want that on the record before we get to the conclusion.

THE COURT: You mean orders for me to sign?

MR. WIESEN: That's the way we had drafted it.

THE COURT: It's fine. If they're drafted that way, you can leave them that way. We'll also just give them exhibit numbers so I can find them.

MR. WIESEN: That's fine. I can hand those up at the next break. I just want to make sure we took care of that before we reach the conclusion of his testimony.

THE COURT: Okay.

MR. WIESEN: The plaintiffs will call Dr. George Gokel

to the stand.

THE COURT: All right, Dr. Gokel.

GEORGE GOKEL,

called as a witness by the plaintiff,

having been duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. WIESEN:

MR. WIESEN: If I could have just a minute to get organized, your Honor?

THE COURT: Sure. Do you want to take five minutes?

MR. WIESEN: If would could have five minutes, that would be helpful.

(Recess)

(In open court)

THE COURT: You may proceed.

MR. WIESEN: Thank you, your Honor. And just for the record, we've handed up some notebooks for you and the Clerk that contain unredacted exhibits. We have a similar situation with Dr. Gokel, some redactions, and we'll try and note that. There may be one or two that we're still negotiating the redactions, and so we'll need to submit a later redacted version for the public record afterwards. We've began talking about it. I think we've worked everything out.

THE COURT: That's fine, great.

BY MR. WIESEN:

Q. Good average, Dr. Gokel.
A. Good afternoon, MR. Wiesen.
Q. Could you please state your name and address for the record?
A. Yes. George Gokel. I live in Chesterfield, Missouri.
Q. What's your field of expertise, sir?
A. I'm a trained as a chemist, and I have expertise as biological chemist and in biophysics.
Q. Before we talk about your background, I just would like you to briefly introduce the topics of your anticipated testimony, and if we could have the first slide, please?
A. Yes. I anticipate speaking about the background of the technology, including co-polymer-1 and the process that are used to prepare these materials, and then I'd like to apply the claims in the defendants, to the defendants' products, and that will involve comparison of the ANDA process to the process limitations of the patents-in-suit, and the comparison of the product to co-polymer-1.
Q. And, sir, were you here for the testimony of Dr. Lisak and Dr. Grant?
A. Yes, I was here for both.
Q. And for that final analysis, do you intend to rely, at least in part, on the expert testimony provided by those witnesses?
A. Yes, I do.

Q. Are you currently employed, sir?
A. Yes, I am.
Q. Where are you employed?
A. I'm employed at the University of Missouri in St. Louis.
Q. What position do you hold at the University of Missouri in St. Louis?
A. My title is Distinguished Professor of Science, and I'm also Director of the Center for Nano-science.
Q. When did you first start working at the University of Missouri in St. Louis?
A. Five years ago.
Q. Where were you before that, sir?
A. I was at the Washington University School of Medicine in St. Louis.
Q. What was your last position there?
A. I was Director of the program at chemical biology and I was Professor of Pharmacology and Biological Chemistry.
Q. How long were you at Washington University in St. Louis?
A. Little under 15 years.
Q. Where were you before that?
A. I was at the University of Miami in Florida.
Q. Could you outline your educational background for the Court?
A. Yes. I received my Bachelor of Science degree with major in chemistry at Tulane University in 1968, and I received a

doctorate in chemistry from the University of Southern California with an emphasis in organic chemistry in 1971. I then spent two years at UCLA in the laboratory of the late Nobel Laureate, Donald Cram.

Q. Did you do a Ph.D. dissertation?

A. Yes, I did.

Q. What was the focus of your doctoral thesis?

A. I was developing certain compounds called ferrocene alkyne molecules, which are -- which are used as asymmetric induction agents for four component peptide synthesis.

Q. Does that have anything to do with synthetic peptides?

A. Yes, it does.

Q. I'm not going to ask you what it has to do with it, if that's okay. Have you taught during your --

A. I beg your pardon?

Q. Have you taught during your career?

A. I'm sorry, I thought you said have I talked. Yes.

Q. What have you taught, sir?

A. I've taught really the entire gamut of courses from undergraduate to graduate. I typically teach now sophomore organic chemistry, and I alternate that with graduate courses in various disciplines.

Q. Do you do any research currently?

A. Yes, I do.

Q. Do you have a laboratory?

A. Yes, I do.
Q. How big is your research lab?
A. If you mean how many people am I currently working with?
Q. Yes.
A. It's nine.
Q. And what's the major area of research currently under way in your laboratory?
A. My major interest is in compounds that enter and alter the properties of biological membranes especially to form channels, and we're interested in molecules that are synthetic peptides and also synthetic (phonetic) enphofiles.
Q. And has your lab conducted research in peptide chemistry?
A. Yes, it has.
Q. How many synthetic peptides would you say have been created in your labs over the years?
A. Hundreds.
Q. Have you supervised any doctoral students or post doctoral fellows?
A. I have supervised both.
Q. How many people, approximately, have gotten Ph.D.'s under your supervision?
A. Approximately 40.
Q. Are you the inventor on any United States patents?
A. Yes.
Q. About how many?

A. About 15.
Q. Sir, over your career, have you received any awards for your research?
A. Yes, I have.
Q. Could you just identify a few of them for the Court?
A. Yes. I was elected a fellow of the American Association for the Advancement of Sciences, and I received the Izatt-Christensen International Award in Macrocyclic chemistry. I received the American Chemical Society's Midwest Award, and when I turned 65 -- when I turned 60, the New Journal of Chemistry did a special issue for my birthday. Oh, and I'm leaving next week to get the Chancellor's award in research creativity.
Q. What is the Chancellor's award in research creativity?
A. It's an award that's given within the University system for achievement.
Q. Have you served on any editorial boards or journals during your career?
A. Yes, I have. I've founded two journals and I've served on about a dozen boards.
Q. And have you served as a referee on any journals?
A. I've served as referee on dozens of journals.
Q. Just briefly, what is the role of a referee on a journal?
A. A referee is someone who one hopes reads the paper with care, and sometimes sympathy, and tries to identify whether

there are flaws in it or whether it has specific problems, and especially is it appropriate in modern times to have an impact on the science.

Q. Have you given any invited lectures, sir?

A. Yes, I have.

Q. Approximately how many?

A. Little over 350.

Q. Did you have any scientific publications in peer-reviewed journals?

A. I do.

Q. Approximately how many?

A. Roughly, I've edited or written about ten books and I've published about 450 papers.

Q. Sir, are you involved in any NIH study groups?

A. Yes. I've been a member of study sections for a number of years, and I'm currently a permanent member of the so-called SBCA, which is the biological chemistry study section.

Q. What do you do as a member of the biological chemistry study section?

A. Three times a year we typically receive about 70 to 100 proposals from other scientists, and we're asked to evaluate them and rate them, and offer detailed opinions about them to try to determine which are the ones most appropriate for funding.

Q. Do you have any experience, sir, working in industry?

A. Yes, I do.
Q. Could you describe that experience for us, please?
A. Yes. After I finished my post-doctoral work at UCLA, I spent a summer at the DuPont central research station in Delaware.
Q. Have you done any consulting in industry?
A. Yes, I have.
Q. Could you describe that for us, please?
A. Yes, I've consulted for quite a number of companies over the years, and in a variety of areas, both in the United States and in England.
Q. Do you have your direct examination binder there in front of you?
A. Yes, I do.
Q. Could you turn to tab 774, PTX-774?
A. Yes, I have it.
Q. Do you recognize this document, sir?
A. Yes, it's a curriculum or biographical sketch that is, that was current about March of 2010.
Q. As of March of 2010, at least, did it accurately reflect your experience in publication?
A. I believe so.
MR. WIESEN: Your Honor, plaintiffs would offer PTX-774 into evidence?
MR. ANSTAETT: No objection, your Honor.

MR. DOYLE: No objection, your Honor.

THE COURT: Admitted.

(Plaintiff's Exhibit PTX-774 received in evidence)

MR. WIESEN: Your Honor, plaintiffs offer Dr. George Gokel as an expert in the field of chemistry, including synthetic and peptide chemistry.

THE COURT: Any objections or voir dire?

MR. DOYLE: No, your Honor.

MR. ANSTAETT: No objection, your Honor.

THE COURT: Then I accept Dr. Gokel as an expert.

THE WITNESS: Thank you.

Q. Thank you.

Dr. Gokel, you were here yesterday for Dr. Grant's testimony?

A. Yes, I was.

Q. And you heard his tutorial at the beginning of his testimony on the polymerization process and the basics of amino acids?

A. Yes, I did.

MR. WIESEN: With your indulgence, your Honor, we want to retread the ground a little bit because there's going to be a little bit more detail in Dr. Gokel's testimony, if that's all right?

THE COURT: All right.

Q. Did you help the lawyers along with Dr. Grant to prepare

some slides?
A. Yes, I did.
Q. Could we have the -- do we have slide number four, please? Sir, do you recall Dr. Grant's testimony about amino acids?
A. Yes, I do.
Q. And if you could just briefly repeat what is an amino acid?
A. Amino acid is a compound that contains an amino group and carboxylic acid.

The basic backbone of organic chemistry is carbon, and other materials such as the amino group and the carboxylic acid are usually referred to as functional groups and they alter the properties of a simple carbon chain. When we add an amino group and a carboxylic acid to this carbon chain, we form what's called an amino acid.

Q. If we could have the next. Now, could you explain what you've done in drawing the graphic to represent amino acid?
A. Yes. In trying to sort of simplify the chemical structure so that we could represent them in a way that will allow us to do multiplicity associated with polypeptides, I've represented them just as a circle around a bowl, it looks like. And I've added a Pentagon and a wedge to indicate that these are the binding positions for the amino group and for the carboxylic acid, amino in blue and carboxylic acid in red. And these are the junction points that will allow the polymer to grow from each of these individual species.

Q. Could we have the next slide, please. How many aminos acids are there, sir?
A. There are many many amino acids. Most proteins known are made from what are called 20 common amino acids, and of these all but glycine have a group here that is different from hydrogen.
Q. Again, what does the R stand for on slide number five?
A. R is -- in chemistry we call it a residue, just -- it means there's something there that's undefined. And so by identifying R, since the framework of these amino acids is all the same, if you know R, you know the identity of the molecule.
Q. Sir, which four amino acids make up co-polymer-1?
A. Alamine, glutamic acid, lysine and tyrosine.
Q. We jumped ahead on you. I apologize.
A. Thanks for the help.
Q. Could we have the next slide, please. Could you explain the structure first of glutamic acid?
A. Yes, I can. I note again that the backbone is exactly the same, R one here has what's called a side chain or pendent group. And if you could show what that is. It has a second carboxylic acid group. So this particular amino acid has the backbone, but it has two carboxylic acids. And I've tried to represent that by showing the linking points that will make the chains and the secondary position here. That is the dangling or pendant carboxyl group.

Q. And can the second carboxyl group have an impact on glutamic acid during polypeptide synthesis.
A. Yes, it can. Because as chains form, the nitrogen bonds to another carboxyl group, and nature doesn't know, if there are two, which one to use.
Q. How would a chemist address that if they wanted to ensure that there was a bond only to one of the two carboxyl groups?
A. Well, we simply eliminate the possibility by putting on here what we call a blocking or a protecting group, then we have only a single carboxyl group that allows the chain to grow.
Q. Could you explain the structure of lysine?
A. Again, lysine has exactly the same backbone of the alpha amino acid, but it has an amino group attached at the end of this chain, and that amino group is now represented by a second pentagon, showing that there are two of these residues that can be used to construct the long chain of polypeptides.
Q. And does the second amino group and lysine create the same issue as the second carboxylic acid group in glutamic acid?
A. It creates the same kinds of issue, yes. It could compete because if a reaction is occurring, nature won't know what -- whether to use this one or this one. Chemistry is just a matter of molecules bumping into each other.
Q. Could you explain, briefly, the structure of alamine?
A. Yes. Alamine is simpler, and it has just a carbon with

three hydrogens. We call that a methyl group.
Q. Does alamine create any problems that require protecting groups in the synthesis of co-polymer-1?
A. No, it does not.
Q. And could you finally explain, just briefly, the structure of tyrosine?
A. Yes. Tyrosine has attached what's called a phenol. It is a hydroxy benzene. It is a reactive compound, but it is not reactive enough to worry about protecting in this case. And so I've illustrated just the main chain linkers here and here.
Q. Thank you. If we could have the next slide, please. Now, briefly, just how do polypeptides form, what bonds with what?
A. Well, the carboxylic acid residue will link with the amino group by the elimination of H2o or water. There are a lot of ways to do that, but that's just the components of the reaction.

So when this is in the presence of another amino acid and all the conditions are appropriate, it will form a linkage by elimination of water to form what's called a peptide bond.
Q. What is a peptide bond, sir?
A. The peptide bond is this structural element or this linkage here that joins together two amino acids.
Q. If you could just describe how you illustrated the top what it looks like, when the two amino acids link together?
A. Yes. I've used, I've used the amino and the carboxylic

acid pentagon and wedge to show that we're building the main chain by inserting those groups into each other. We don't show the loss of water, but that's understood by a person who is skilled in the art.

Q. Could we just play out the rest of this slide, please; what are you showing here?

A. Here we add alanine to form a new peptide bond. R3 is alanine, and here we add the tyrosine derivative, so we have three peptide bonds, four amino acids. And even though it doesn't look this way, we call this a straight chain or a linear chain, because there is a linear chain of atoms connecting all these. Sometimes this is called the main chain.

Q. Would you be sure to have that straight linear chain if you didn't put protected groups on glutamic acid or lysine?

A. If you didn't have protecting groups on these secondary carboxyl or amino functions, then the chain could grow from either of these, and we would have what we call branching.

Q. Have you prepared a slide to illustrate that possibility?

A. Yes. This would be the normal straight chain growth using only the main chain, the NC. NCCNCC arrangements that forms the amino acids. If we have unprotected linkages, however, we can grow bonds downward by bonding to other species, and we could have even more complex structures than what's illustrated schematically here.

Q. Now, have you illustrated how a chemist would prevent that

from occurring in the synthesis of co-polymer-1?
A. Yes, I have. For glycine, remember we have a correspondence --
Q. Sir, do you mean glutamic acid?
A. Sorry. By chemistry G means glycine. Sorry. Glutamic acid has carboxylic acid here and carboxylic acid here. So in order to have main chain growth, we need to block or protect this. And I've tried to illustrate the protection by using this circle. And this represents what's done in the '808 series of patents. It is protected with a benzyl group.
Q. Are there other protecting groups that could be used to protect that site on glutamic acid?
A. Yes, there are many, many protecting groups are known that could be used.
Q. And what protecting group is used in the '808 patent for lysine; how do you illustrate it?
A. For lysine, I've used a color coded square box, and I've used the trifluoracetyl group as a protecting group because that's what's used in the '808 patent.
Q. And are the protecting groups different on the lysine and the glutamic acid?
A. Yes, the protecting groups are different. Glutamic acid, it's benzyl from a choice of many, and in lysine it is trifluoracetyl for a choice of several groups that could be used there as well.

Q. I want to turn now to the same animation that Dr. Grant presented yesterday on polymerization, and just ask you if you could briefly explain this, now that we've added in the explanation of what the little boxes and circles at the bottom of the glutamic acid and the lysine are?

A. Yes.

Q. And would it be easier for you, sir, to step down to do it; are you comfortable doing it from there?

A. I think I can do it from here. Let me, before we do any animation, let me just remind everybody that this is a blocked or protected lysine. This is a blocked or protected glutamic acid. All of these materials have what were called earphones yesterday, I was calling them pale handle but it's the same thing. It's a schematic representation to show the end carboxyl hydride, which is the way these molecules are activated. If we just mix together amino acids, they wouldn't react. Even if we mix together the activated amino acids, they don't react very readily until we add a molecule that's called an initiator. When we do that, it bumps into one of these molecules at random, and when it does that, the -- could we stop for a moment? You can see that the activating groups go away as the chain is formed, but the protecting groups do not. Could you please continue?

And as these various initiators react, we get compounds of different lengths and of different sequences. I

think there will be several molecules shown by the end of this animation.

So this represents the fact that in this particular process we have an initiator that begins the reaction, but we have random sequences, and we have a range of different lengths. Of course the actual molecules are significantly longer than this, but we've made it a little smaller so that it can be seen on the screen.

Q. Now, are there significantly more molecules than the actual mixtures, sir?

A. Oh, yes, many more molecules in the actual mixture; about a million, billion.

Q. Is there a name for this process in chemistry?

A. Yes. This process is often called polymerization because we have an addition of one monomer to another monomer to another monomer.

Q. And just to make sure it's clear, sir, do the polypeptide chains in this process at the end of the polymerization step have the same lengths?

A. No, they do not. There may be some that do have the same length, but in general, it's a whole variety of different lengths, and that's what's intended to be represented here.

Q. And so the record is clear, do the polypeptide chains as part of the polymerization process have the same sequence of amino acids?

A. No. I've also tried to represent random sequences to show that it's not clear which amino acid will react with the next one.

Q. And, sir, do you recall what name the patent gives the compound at this point in this synthetic process?

A. Yes, I do. Because we still have protecting groups on the lysine and protecting groups on glutamic acid, it's called protected co-polymer-1.

Q. Are those protecting groups left on glycine and glatiramer acid at the end of the process to make co-polymer-1?

A. No. The sequence deliberately removes them.

Q. What's the next step in the sequence for making co-polymer-1?

A. This mixture of polymers is then treated with a mixture of chemicals called HBR. That process removes the benzyl groups from the glutamic acids, but not from the lysines. It also has the effect, as is clear from this title, deprotection, depolymerization, that it also leaves some of these chains. And I've indicated that with these runic acids to show there are cleavage points throughout the molecules. So what happens is we remove these protecting groups that are on the glutamic acids and we also cleave to shorter chains.

Q. And do some of the documents call this a depolymerization stop?

A. They do. It can be called a depolymerization or cleavage,

or sometimes it's also called a lysis.
Q. What happens to the length of these polypeptide chains when they're caught by the HBR acidic acid stop?
A. Well, of course, they were longer, so when they're cut they become shorter.
Q. And, sir, what happens to the average molecular weight of the mixture of polypeptides when this cleavage occurs?
A. Well, as the chains get shorter, the average molecular weight of each chain goes down, and so the average molecular weight of the mixture diminishes.
Q. And is there a name to this synthetic process for the result of this step to deprotection, depolymerization or cleavage step?
A. Well, the product that results from this step is called in this process, trifluoracetyl co-polymer-1. Because it is still co-polymer-1, although reduced in molecular weight, it still contains the protected lysines which are protected as this trifluoracetyl group.
Q. What's the next step in the synthesis of co-polymer-1?
A. Well, the next thing is that we need to remove the protecting groups that were on lysine, and we do that by treating with a chemical called piperidine.
Q. And when treating with piperidine, is the chain length of the polypeptides affected?
A. No. This step is different from the first step, in that

respect. It has no effect on the chain length. It simply removes the protecting groups that are on lysine.

Q. And, sir, what's the result of this, excuse me, deprotection with piperidine, what's the resulting compound?

A. At this point, we have polymerized the molecules, we have cut the chains, we've removed the glutamic acid protecting group, and we have now removed the lysine protecting group and we get a polymer mixture or a peptide mixture that's described as co-polymer-1.

Q. Is there any protecting groups left on the final co-polymer-1 molecule?

A. No.

Q. Thank you. I want to turn then to the '808 patent and example four for a minute. But before we do, could we have the next slide, please.

You were here yesterday when Dr. Grant gave testimony concerning the level of skill of a person of ordinary skill in the art?

A. Yes, I was.

Q. And on slide 21, we've put up the level of skill the person of ordinary skill in the art Dr. Grant discussed.

Did you apply this definition of person of ordinary skill in your analysis today?

A. Yes, I did.

Q. You agree with this as the appropriate level of ordinary

skill for this case?

A. Yes, I think it's very reasonable.

Q. If you could turn to PTX-1 in your binder, the '808 patent?

A. I have it.

(Continued on next page)

Q. You reviewed this document as part of your work in this case, sir?
A. Yes.
Q. I want to turn to example 4, columns 4 -- actually, columns 4 through 6, although we've prepared a slide that pulls out all of example 4. Did you help make this slide, sir?
A. Yes, I did.
Q. Do you recognize this as example 4 from the patents?
A. Yes, I do.
Q. Could you briefly explain how example 4 compares to the tutorial we just ran through on the synthesis of copolymer-1?
A. Yes. Overall what I've tried to do is to correlate the tutorial we just talked about with the actual words of the patent. So protected copolymer-1 is made from the activated amino acids by reaction with an initiator called diethylamine that results in protected copolymer-1.
Q. Could we click so we can see the next one, too?
A. Once we have protected copolymer-1, we need to remove the protecting groups or blocking groups that are present on the glutamic acids and we treat with HBr acetic acid. During that process, we also have a reaction that occurs, and I've indicated that again with this red S that allows us to cleave the chains. So the S just indicates that the blocking groups that were here are now gone and this assemble tells us we cleaved.

The next step, we have trifluoroacetyl copolymer-1 in shorter chained structures, but we still need to move the protecting groups that are present on the lysines. We do that by treating with piperdine and piperdine again we show X's to indicate the removal of those groups and that gives us the polymer mixture that we know is copolymer-1, which is now shorter chained than it was at the beginning and also free of the protecting groups that were present at the beginning. This is copolymer-1.

Q. Does example 4, sir, also include some additional purification steps that we did not illustrate in the tutorial?

A. Yes, they do. What I've listed here as step -- sorry, didn't get it high enough -- this step 8 and 9. The step 8 is treatment called dialysis which is a purification step and that yields in 9, purified copolymer-1.

Q. Thank you, sir. Now that we've run through the tutorial and the basic description in example 4, I want to turn to the manufacturing processes proposed to be used by the two defendants in this case, Sandoz and Mylan. Have you looked at documents concerning Sandoz and Mylan's processes?

A. Yes, I have.

Q. And first focusing on Sandoz process, do you have an opinion as to whether the process limitations of the patents in suit, and we'll get to those later, are met by Sandoz' process?

A. Yes, I do.

Q. What is your opinion, sir?
A. I believe that the Sandoz process does meet the process limitations of the patents in suit.
Q. Let's look at some of the documents from Sandoz' and try to break that down a little bit. If you could turn to PTX 216 in your binder?
MR. WIESEN: This is a document, your Honor, that has been redacted for the public record. You have a complete copy.
A. So mine now says 216R.
MR. WIESEN: What we've done, your Honor is for the redacted copy --
THE COURT: The same system we used before?
MR. WIESEN: Correct.
THE COURT: So the witness has the redacted. Okay.
THE WITNESS: I understand.
Q. Dr. Gokel, have you reviewed this document or actually the unredacted version of this document, in rendering your opinions in this case?
A. Yes, I do.
Q. Is this document part of Sandoz' ANDA?
A. That's my understanding.
MR. WIESEN: Your Honor, plaintiffs offer PTX 216 into evidence.
MR. DOYLE: No objection, your Honor.
THE COURT: Thank you, 216 is admitted.

(Plaintiff's Exhibit 216 received in evidence)

Q. What is the title of Sandoz' ANDA, if we left the title on? If you could turn to page SDZ 1937?

A. Yes, I'm there. It's Section 3.2.S.2.2 is titled description of manufacturing process and process controls (glatiramer acetate).

Q. Very briefly, what's illustrated in this diagram we've called out from the page?

A. This is what chemists call a synthetic scheme or a synthetic overview which allows a person of skill in the art, a chemist, to look at the various steps that will be performed to get from A to B to C, whatever it is, and the reagents are typically put in some sort of shorthand over arrows and the arrows indicate that the sequence is proceeding in the indicated direction.

Q. And, sir, I know there have been some minor changes in Sandoz' process set forth in their ANDA. Has this basic synthetic scheme stayed the same throughout the time their ANDA has been pending?

A. Yes, it has.

Q. Have you prepared some slides to show how this synthetic scheme compared to the scheme disclosed in example 4 of the patent?

A. Yes, I have.

MR. WIESEN: Could we go back to the slide, Mr. Chase?

If we could have the next slide, please.

Q. Before we get started with this synthetic scheme, could you explain what the four boxes are at the bottom of this diagram?

A. Certainly. Each of the amino acids was designated as having an R or residue group and they're different, so they have R1 or R2 or R3 or whatever. Here we have lysine, alanine, glycine and tyrosine, so those side chains that were represented before with R1 are shown to illustrate what is the substituent on the amino acid. This is a generalized structure for all of them, and this seeks to illustrate what each of the individual ones is at this stage. So glycine is clearly protected with the benzyl group and lysine is protected with the trifluoroacetyl group. Alanine and tyrosine are unprotected. At this stage this is the N carboxyanhydride.

Q. Sir, when you said glycine, again, do you mean glutamic acid?

A. I'm sorry, yes.

Q. If you could just explain to the Court for a minute why it is that, what different abbreviations economists sometimes use or generally use for amino acids?

A. I apologize. These amino acids are abbreviated in single letters as AEKY, that's what we learn in school. So alanine actually is abbreviated as A in standard terminology, but G is glycine, L is leucine and T is threonine. So I think, I'm trying not to -- I'm trying not to screw up.

So I apologize and please catch me when I do that. So this is glutamic acid, alanine, lysine and tyrosine.

Q. If we could quick through, Mr. Chase. You indicated the different protecting groups in the different stages of the amino acids for the different parts of the process in these slides?

A. Yes. So at this particular stage you can see that the benzyl group has been removed from the glutamic acid but that the lysine remains protected, and at this stage the glutamic acid is simply present as a salt and the lysine protecting group, trifluoroacetyl, has been removed and then here at the end, we have the free carboxyl, the methyl group which was never protected, the tyrosine which was never protected, and the amino group which is formed as a salt with acetate or acetic acid.

Q. Have you prepared a slide illustrating how these steps in the synthetic diagram match up to the steps in example 4 of the '808 patent?

A. Yes, I have.

Q. What's portrayed here on slide 30?

A. What I've tried to do here is to correspond the synthetic scheme from Sandoz' with the nine points that I showed in the sequence from example 4 of the '808 patent. So we begin with the N carboxyanhydrides. Those are the starting materials with the earphones or pail handles, whatever you want to call them.

Those are allowed to react with the initiator which is diethylamine.

Q. What initiator does Sandoz' use in its process?

A. Diethylamine.

Q. Continue, please.

A. That initiates the polimerization process that gives us these long chains of protected amino acids. And we then treat with HBr in acetic acid, here's the HBr acetic acid. That cleaves these chains to remove the protecting groups that were on the glutamic acid and it also cuts the chains in the same reaction.

Q. And, sir, was it known before these patents that HBr acetic acid would controllably cleave polypeptide chains?

A. No, it was not. It was known that HBr and acetic acid was a useful reagent to remove the benzyl group, but the cleavage of peptides would be a nuisance.

Q. You could continue with Sandoz' synthetic process, please.

A. Yes. So we're at stage 5 here where we have the trifluoroacetyl copolymer where we have protecting groups on the lysines and we have shorter chains now. And that gives us trifluoroacetyl copolymer-1. In order to remove these residues, we treat with piperdine in water and that gives us the next stage, the removal of these protecting groups, but it does not affect the molecular weights of the individual chains.

Q. And so what does Sandoz use in its process to remove the

protecting groups on the lysine?
A. Sandoz uses piperdine as is used in the '808 patent.
Q. Would you continue describing what you have on slide 38 now concerning Sandoz' synthetic process?
A. We now have a large number of these shorter chains that have been deprotected both at the glutamic acid and at the lysine and that gives us the product called copolymer-1 and here it's illustrated as a piperdine salt, simply meaning that the piperdine reagent has neutralized the carboxylic acid.
Q. How does Sandoz in its process purify that compound?
A. They do it by what they called diafiltration, which is like the dialysis in the '808 patent.
Q. And what's the last step?
A. In the last step they obtain the purified copolymer-1 as the acetate salt.
Q. Here Sandoz called this glatiramer acetate is that right, in their synthetic pathway?
A. That's right.
Q. Do you have an opinion whether Sandoz' glatiramer acetate is copolymer-1 as the term is used in the patent?
A. Yes I do.
Q. What's your opinion?
A. My opinion is that glatiramer acetate is copolymer-1.
Q. Sir, do you have an opinion whether Sandoz' process is similar to the process disclosed in example 4 of the '808

patent?
A. Yes. I believe it to be similar.
Q. Thank you, sir. There's one other detail I just want to talk about briefly that we'll need when we get to particular claims in Sandoz' process. If you could turn back to PTX 216 to SDZ1949.
A. Sorry, what was the page number?
Q. 1949 and we'll call outline 8, please.
THE COURT: What was the exhibit? I'm sorry?
MR. WIESEN: 216, your Honor.
A. I have it.
Q. What do steps 8 and 9 indicate on this page for Sandoz' process?
A. It says to prepare an acetic acid solution in a separate vessel by adding acetic acid to purified water and then add that solution to achieve a certain pH.
Q. Is this during a certain purification stage of Sandoz' synthetic process?
A. Yes, it is.
Q. Now, if you could turn to PTX 213 in your binder.
A. I have it.
Q. This is another document, your Honor, that's been redacted.
A. All right.
Q. And did you review the unredacted version of this document in rendering your opinion?

A. Yes, I did.

MR. WIESEN: Plaintiffs would offer this exhibit as well. I'm not sure at this point whether it has or has not yet been offered.

THE COURT: Any objection?

MR. DOYLE: None, your Honor.

THE COURT: All right. Admitted.

Q. What is this section of Sandoz' ANDA entitled?

A. This is Section 3.2.S.4.4. It's entitled "Batch Analysis Glatiramer Acetate SAFC Pharma."

Q. If you could turn to SDZ2421 please?

A. I have it.

Q. What is this document, sir?

A. This is a certificate of analysis on Momenta stationery.

Q. And I think we've heard -- well, first, do you know the relationship between Momenta and Sandoz for the purposes of this case?

A. It's my understanding that they are collaborators.

Q. I think we've heard some discussion about a certificate of analysis before, but could you tell us what a certificate of analysis is?

A. Yes. One sets up limits that are allowed for the purity of various molecules. You need to be sure you have the right molecule and you have to have a number of ways to tell that, and you also want to know if you have various impurities.

Standards are set for those, analytical methods are applied and you try to see if you have fallen within the limits that you desire.

Q. If we look at the line tabled TP116, just pull that out. Do you have an understanding what this is a specification for?

A. Yes. It's titled "molar mass" and it says that the molecular weight is 5,000 to 9,000 daltons.

Q. In your opinion, sir, and Dr. Grant may have discussed this yesterday, I apologize, do you have an opinion whether this is a predetermined molecular weight profile in the Sandoz and Momenta ANDA?

A. Yes. The acceptance criteria is specified there, so is a predetermined molecular weight.

Q. Just for the record, I want to turn briefly to an update that Sandoz had provided. If you could turn to PTX 353 in your binder.

A. I have it.

Q. I'll ask you whether you recognize this as the document you've reviewed to prepare your -- is it the unredacted document that you reviewed in preparing your opinions in this case?

A. Yes. Yes, I recognize it. A lot's been removed.

MR. WIESEN: Your Honor, this is another document that obviously has redactions. We'd offer PTX 353 into the record.

MR. DOYLE: No objection.

THE COURT: No objection, admitted.

(Plaintiff's Exhibit PTX 353 received in evidence)

Q. We don't even need to call out any of the details, Mr. Chase. Could you just confirm that in the updates the basic synthetic process we talked about has not changed in Sandoz' process?

A. Yes, I could confirm that.

Q. Thank you. Your Honor, we're going to move now on to -- actually, I have one more thing to do on this one, sorry.

Now, Dr. Gokel, do you have an understanding of whether Sandoz or Momenta considered alternative processes to prepare copolymer-1?

A. Yes, I do.

Q. Did they consider alternative processes?

A. Yes, they did.

Q. If you turn to PTX 141 in your binder.

A. Yes, I have.

Q. Do you recognize this document, sir?

A. Yes. This is a presentation that was made to a meeting in December of 2005 and the author is listed as Mani Iyer.

Q. Did you review this document in rendering your opinions in this case?

A. Yes, I did.

MR. WIESEN: Your Honor, plaintiffs offer PTX 141 into evidence.

THE COURT: Any objection?

MR. DOYLE: No, your Honor.

THE COURT: Admitted.

(Plaintiff's Exhibit PTX 141 received in evidence)

MR. WIESEN: Thank you.

Q. Could you turn to the page bearing the Bates labeled MMT 00391608?

A. Yes, I have it.

Q. Do you have an understanding of what this page refers to?

A. Yes. My understanding of this is that the presenter was offering strategies for the active pharmaceutical ingredient, approaches to manufacturing it, and he offers, I believe Mani is he, offers Phase I, Phase II and Phase III plans.

Q. Excuse me, do you have an understanding of whether the Phase I plan, what the Phase I plan is?

A. Yes. My understanding of the Phase I plan, assimilate technology, it says replicate literature process. That means in short, copy the patent.

Q. And do you have an understanding of what Phase II is?

MR. DOYLE: Objection, your Honor. Move to strike. This is speculation in terms of this witness' knowledge of what --

THE COURT: Right, well, I don't hear any foundation for it. All right. Sustained.

Q. Do you have an understanding of whether Sandoz/Momenta's

process replicates the literature process?
A. If I assume the literature process is the '808 patent, it duplicates that, yes.
Q. Let's look at Phase II for a moment. Plan A, keep it simple. Do you have an understanding of what that is?
A. Yes.
MR. DOYLE: Same objection, your Honor.
MR. WIESEN: I'll ask a more specific question.
THE COURT: Okay.
Q. Looking at the first bullet point under Phase II, minimally modify NCA-based process. Has Sandoz and Momenta's process modified the NCA-based process in any way from the process described in the '808 patent?
A. No.
Q. And looking at the Phase III, plan B, contingency plan, has Sandoz/Momenta's process provided any alternate coupling non-NCA methodologies compared to the process in example 4 of the '808 patent?
A. Their current methodology uses an NCA methodology for coupling, as does the '808 patent.
Q. If you could go to the third bullet under Phase II, if you could just read that into the record please, sir?
A. Stay outside the process claims.
Q. If you could go to the second bullet under Phase III, could you read that into the record, please?

A. It says adds additional distance from a IP standpoint.
Q. Thank you, sir.
MR. WIESEN: Your Honor, we're going to transition now to the Mylan process. It might be a natural time to take a break for lunch.
THE COURT: Fine. Why don't we adjourn until 1:45, get a few extra minutes in.
(Luncheon recess)
o0o
AFTERNOON SESSION
(2:00 p.m.)
THE COURT: You may proceed.
Q. Good afternoon, Dr. Gokel.
A. Good afternoon.
Q. The danger of the lunch break, I was told I skipped over a couple of slides. So I very quickly want to go back to slide 41 in the Sandoz process. Did you help prepare some slides, sir, to show thousand the reactions and reagents in the Sandoz process compare to those in example 4 of the patent?
A. Yes, I did.
Q. Are the reaction and reagents in Sandoz' synthetic process the same as those in example 4 in the patent?
A. Yes, they are.
Q. Would you describe what you have starting on slide 41, please?

A. Yes. This box represents the three steps that are the transformation from the activated amino acids reaction with the initiator diethylamine to the initial dye protected copolymers.
Q. Could we have the next slide, please?
A. Treatment with HBr acetic acid then removes the benzyl-protecting group and then depolymerizes or cleaves or chops up the chains so we get more shorter chains and we also have no more benzyl groups on the glutamic acid residues.
Q. If we could have the next slide, please. What do you show here on slide 43?
A. The final deprotection step is done with piperdine and water, which removes the trifluoroacetyl protecting group to give copolymer-1.
Q. Thank you, Dr. Gokel. Did you also look at Mylan's synthetic process?
A. Yes, I did.
Q. Do you have an opinion whether Mylan's sympathetic process made copolymer-1 in its proposed ANDA would meet the process limitations in the asserted claims in this case?
A. Yes. I believe that it does.
Q. Thank you. If you turn to PTX 321 in your binder. Have you reviewed this document, sir?
A. Yes, I have.
Q. And is this document a portion of Mylan's ANDA?
A. That's what I understand it to be.

MR. WIESEN: Plaintiffs would offer plaintiff's PTX 321 into evidence. This one is one that we will prepare a redacted public version, but it's not been prepared yet as we've been talking with Mylan's counsel about what needs to be redacted.

MR. AANNESTAD: Subject to counsel's representation on that confidentiality issue, we have no objection.

THE COURT: It is admitted with that understanding.

MR. WIESEN: Thank you, your Honor.

(Plaintiff's Exhibit PTX 321 received in evidence)

Q. What's described in this portion of Mylan's ANDA, sir?

A. This is the synthetic process and beginning at page MYL 0000251 there is the same type of schematic that we looked at before for the Sandoz process.

Q. And, sir, have you similarly prepared some slides to show the synthetic process in example 4 as well?

A. Yes, I have.

Q. Would you go to those slides, please?

A. Yes. These four slides represent the overall synthetic process as presented in Mylan's ANDA.

Q. Just for the record, these slides are MYL251, MYL252, MYL253 and MYL254. If we could just pull up the next slide please. What's on MYL254?

A. This is a list of abbreviations that Mylan uses in their processes. It's customary in industrial enterprises for local

abbreviations to be used so that people know what they're talking about without having to say full names like carboxyanhydride pyridine.

Q. And has Mylan used these abbreviations in the pages we're going to look at?

A. Yes, they do.

Q. Could we go to the next slide, please? What step of Mylan's process is shown here in slide 47?

A. This is the initial step in which the four N carboxyanhydride derivatives -- this one is glutamic acid. It has a benzyl protecting group indicated by BZL, the abbreviation. This is the alanine NCA. This is the lysine protected by trifluoroacetyl with an indicated TFA here and this is the activated tyrosine form.

Q. Have you illustrated those?

A. I beg your pardon?

Q. Could we have the next slide, please? First let me back up a second. What's made as a result of this process?

A. Well, what's indicated here by this arrow, which doesn't have any reagent associated with it is polymer benzylated glutamic acid, alanine, tyrosine, lysine protected by TFA so it's this the polymer that we would call protected copolymer-1 they call GAM F1.

Q. Could we have the next slide, please? Does this identify -- next slide please as well. Does this identify the

four N carboxyanhydride amino acids that are used in the process?

A. Yes. Analogizing to example four, these are the four residues; glutamic acid protected lysine protected alanine and tyrosine illustrated here with our little icons to show which they are; they are the carboxy, N carboxyanhydrides, same deactivating group on each one.

Q. What initiator does Mylan use?

A. Diethylamine.

Q. Is that shown on this page?

A. It is not.

Q. If you could turn to MYL260. We have a slide prepared for that as well. If you could go to the next slide. What does line 9 on page MYL260 indicate about what initiator is used by Mylan?

A. Line 9 is an instruction to add diethylamine into the mixture. That's the initiator that they use.

Q. What's the result of mixing the initiator and the activated amino acids in Mylan's process?

A. The result is that the initiator causes the formation of the di-protected or protected copolymer-1.

Q. What's the next step in Mylan's process? Is that the next slide?

A. The next step is to treat with HBr and acetic acid to produce trifluoroacetyl copolymer-1. That's shown here. Our

protected copolymer one is treated with HBr and acetic acid and that again cleaves this glutamic acid protecting group and cleaves the polymer chains at the same time resulting in the formation of trifluoroacetyl protected copolymer-1. So this protecting group has been removed and the chains have been shortened, just as we saw in the '808 patent.

Q. And can we see on the formulas that are indicated the fact that the protecting group has been removed from the glutamic acid?

A. Yes. Certainly here glutamic acid is written in parenthesis OBZL to indicate the presence of the O-benzyl protecting group and we see here that it's gone but the trifluoroacetyl group is retained.

Q. And what's the result from this process?

A. The process, from this process we get trifluoroacetyl copolymer-1, which we then treat with piperdine in water to remove this protecting group, this protecting group TFA and the result is the formation of copolymer-1.

Q. Does Mylan also further purify the copolymer-1 substance?

A. Yes, they do.

Q. Where is that indicated?

A. That's indicated here, diafiltration of copolymer to remove piperdine.

Q. And what does Mylan call the final result, lyophilize, if I'm pronouncing it right.

A. Close enough. I'm sorry, I can't see this slide. Would you ask me the question again, please?
Q. What do they indicate by the lyophilize at the end of the process?
A. They obtain and lyophilize copolymer-1.
Q. Just to be clear, what is lyophilization?
A. It's sometimes called freeze drying.
Q. I want to turn to one other step that's in Mylan's process, if you could turn to MYL267 in the exhibit we've been looking at, PTX121.
A. I'm sorry, I missed the page number, please.
Q. Page 267. It's up on the screen as well, sir.
A. Thank you.
Q. In this step of Mylan's process do they add acetic acid as part of the purification process?
A. Yes, they do. The highlighted portions indicates they slowly add acetic acid into the circulation tank.
Q. Thank you, sir. If you could turn, then, to page 294 in your binder.
A. Yes, I have it.
Q. Do you recognize this document?
A. Yes, I do.
Q. If we could pull out line 7. Is this a certificate of analysis for one of Mylan's ANDA batches?
A. Yes, it is.

Q. What's contained on line 7?
A. Line 7 shows molecular weight distribution by size exclusion chromatography. The result is 6,445 and the specification is that the product should be between 5,000 and 9,000 daltons.
Q. In your opinion, sir, based on this certificate of analysis, does Mylan have a predetermined molecular weight profile for its proposed ANDA product?
A. Yes. The specification tells us that they do.
Q. Do you know, sir, whether Mylan considered developing -- well let me back up. Does Mylan's process contain the same reactions and reagents as disclosed in the '808 patent?
A. In my opinion it does.
Q. Do you know whether Mylan considered developing any alternative processes?
A. Yes, I believe they did.
Q. Could you turn to PTX 270, please?
THE COURT: Is 294 already admitted?
MR. WIESEN: I believe it is, your Honor. I believe the certificates of analysis came in with Dr. Grant, I believe.
THE COURT: All right, and this is --
MR. WIESEN: 270, your Honor.
Q. Dr. Gokel, did you review this document preparing your opinions in this case?
A. Yes, I did.

Q. If we could highlight issues and actions at the bottom? Could you read just number 3 into the record now?
A. Yes. It says, "Both non-infringing and infringing processes has to be established in lab first and later transferred to scale-up."
Q. Do you have an understanding of which process from this e-mail Mylan and Natco adopted for their NDA in this case?
A. They adopted the procedure that we've just been talking about, which I believe to be infringing.

MR. ANSTAETT: Your Honor, I have an objection on foundation grounds. I don't think we've established a foundation that Dr. Gokel could know what's referred to in this document.

MR. WIESEN: I'll set a foundation, your Honor.

THE COURT: I think I've heard his answer. There's no code here. I've heard his answer. I understand what's going on. Okay.

Q. Dr. Gokel, did you review Dr. Kota's depositions in rendering your opinions in this case?
A. Yes, I did.
Q. If we could have the next slide, please.

MR. ANSTAETT: Your Honor, I have an objection to this as well. Again, I understand that Mr. Wiesen is trying to establish a foundation, but there's no reference to any patents that are being discussed here, so this deposition testimony,

there's no foundation that it refers to any of the patents.

MR. WIESEN: The testimony has been designated, your Honor. I think it's something Dr. Gokel relied. On it's appropriate for him to explain his interpretation and understanding.

MR. ANSTAETT: The fact the testimony has been designated --

THE COURT: Whose testimony? Would you put it up please?

MR. WIESEN: Dr. Kota, one of the scientists from Natco.

THE COURT: You're going to argue this as an admission? Okay.

MR. ANSTAETT: Whether it's an admission or a statement, there's simply no foundation established by this or any other testimony for any of the patents in suit.

THE COURT: Not by this five lines. I agree with you. Okay.

MR. WIESEN: We'll move on, your Honor.

THE COURT: Okay.

Q. Dr. Gokel, based on your analysis as we've run through it of Mylan's synthetic process, do you have an opinion whether if Mylan's process if used would meet the process limitations that we'll describe in detail later in the claims in the patents in suit?

A. Yes, I do.
Q. What's your opinion sir?
A. I believe the process meets the process limitations of the patents in suit.
Q. I want to turn to another topic, then, sir, the question of whether Mylan's product is copolymer-1 as the term is used in the patents. Are you aware that the Court provided a construction of the term copolymer-1 in this case?
A. Yes, I am.
Q. Have you analyzed whether Mylan's products meets each of the portions of the construction of copolymer-1?
A. Yes, I have.
Q. I've highlighted for you synthesized by polymerization of suitably protected amino acid carboxyanhydrides. Do you have an opinion, sir, of whether Mylan's process would meet this portion of the limitation?
A. Yes, I believe it does, for the reasons that I gave a few minutes ago in the discussion of the synthetic sequence.
Q. Could we have the next slide, please? Do you believe Mylan's process would result in a mixture of polypeptides?
A. Yes, I do.
Q. What's the basis for that opinion?
A. The basis is the same as the analysis that I gave of the overall synthetic process.
Q. Do you have an opinion whether Mylan's proposed product

would be non-uniform with respect to molecular weight and sequence?

A. Yes, I do.

Q. What's the basis for that opinion?

A. Dr. Grant's testimony.

Q. Do you have an opinion whether Mylan's proposed product would be composed of alanine, glutamic acid, lysine and tyrosine?

A. Yes, I believe it would be, because those are the starting materials for the synthetic sequence.

Q. Next slide, please. Do you have an opinion, sir, whether Mylan's proposed product would be in a molar ratio of approximately 6:2:5:1?

A. Yes, I do.

Q. What's your opinion, sir?

A. My opinion is that the product is in a molar ratio of approximately 6:2:5:1.

Q. All right, that one I think we'll probably have to spend a little bit of time on.

So before we start the discussion in detail, sir, what is a molar ratio?

A. A molar ratio is the ratio of certain components within a molecule or a larger structure.

Q. And have you prepared some graphics to help illustrate the concept of a molar ratio?

A. I have.
Q. Could we have the next slide, please? What's shown here on slide 64?
A. Copolymer-1 is composed of alanine, glutamic acid, lysine and tyrosine, and even though there are many different chains and many different links, many different sequences, these are the four amino acids that comprise all of the molecules in the mixture. If you break down the structure, analyze the structure, you find that overall within the structure there are six alanines for two glutamic acids for five lysines for one tyrosine. So the molar ratio is 6:2:5:1 in this demonstration.
(Continued next page)
BY MR. WIESEN:
Q. And what is a mole, sir?
A. A mole is a term that chemists use to define a specific number of molecules that corresponds to its positive molecular weight. It's six times ten is a 23rd molecules, it's gigantic number of molecules. But just think about it like a pound of molecules or something.
Q. All right. How would a chemist go about determining a molar ratio?
A. Well, in a case like this, we would -- we would analyze a product, we would break it down to its components and find out how many of each kind of component there is, and then we would sum it and divide it by the different fragments.

Q. So here on slide 65, what have you depicted?
A. This is a, this is a schematic or sort of an average co-polymer-1. It contains 70 amino acids total. It has a molecular weight of, with this sequence, of little over 7,000, and it's intended to illustrate this random coil arrangement of and non-uniform sequence.

This was, this picture or illustration was constructed from 30 alamines, ten glutamic acids, 25 lysines, and five tyrosines to give us a total of 70 amino acids.
Q. And what would a chemist do then to analyze the molar ratio?
A. One way to do it would be to hydrolyze, that is to say, break each of the carbon, each of the peptide bonds by putting the water back in. The water came out when we had polymerization reaction. We know how to put it back in, and break the molecule up into its fragments.
Q. What do you do next to figure out the molar ratio?
A. Well, we have methods by which we can sort these molecules. Once we know how many different kinds of molecules we have, we can establish the molar ratio.
Q. And how would you -- what would you do once you have the molecules sorted?
A. Well, we have a total of 70 molecules. So in order to find the molar ratio, the proportion of each within this original structure, we would say, okay, let's think about the alanines,

there are 30 alanines, there's 70 total amino acids. If we divide them, we get .43. We could say there are 43 percent. We would do the same with glutamic acid, would be ten over 70 or .14. For lysine it would be 25 over 70, or .36, and for tyrosine it would be five over 70 or .07.

Q. Now, sir, would there be different ways to express the molar ratio of 6:2:5:1 to a person of ordinary skill?

A. Yes. One could express that ratio just as you've done here, .43, .14, those are mathematically equivalent. All we've done in this slide is say there's a whole number ratio of 6:2:5:1. We can express that as a fraction of the amino acids. Six over 14 is .43. We can multiply that by 100 and say on a percentage basis there are 43 percent alanines in the original structure.

Q. Now, I see under the ratio column you have the scale indicated as 14. Where did you come up with that number, sir?

A. Well, the scale for this is 6:2:5:1. And so for a comparison, the scale is 14. And if we want to compare something else with it, we need to be on the same scale. For factions, we would want to compare on a scale of one or unity, because factions are obviously some fraction of unity, and for percent we usually use 100 percent, but they all convey the same information.

Q. And just for the record, with the ratio of 6:2:5:1, approximately what percent of each amino acid is present?

A. Approximately 43 percent is alanine, approximately 14 percent is glutamic acid, approximately 36 percent is lysine, and approximately 7 percent is tyrosine.
Q. Have you also created some pie graphs to show how one skilled could do this comparison?
A. Yes, I have.
Q. What is shown here on slide 68?
A. These are pie charts which encompass the whole molecule. I've set this as scale of 14 and compared it to one. The scale of one is perfectly valid when we said we were talking about fractions, total is unity. The scale of 14 is perfectly valid when we were talking about the numbers of these 6:2:5:1. But it's clear that although the two pictures are different in size, they actually convey identical information slices are just the same positive portion in each case.
Q. Now, sir, if you wanted to, say, convert from the total scale of one the molar fraction to the molar ratio of 6:2:5:1, how would a person of ordinary skill do that?
A. Well, the conversion of these into each other is just multiplication or division. So if we wanted to get these fractions on a scale of 14, we would just multiply each by 14 and we'd get a ratio of 6:2:5:1.
Q. And have you prepared a slide to show the way that a person of ordinary skill in the art would go about comparing things on the same scale?

A. Yes, I have.
Q. What does this slide say?
A. Well, it's perfectly valid to have a scale of one and look at the fractions, compared to this larger stacked plot. It's harder to see the proportions. It's correct if you scale both of those, this one and this one to 14. It's correct if you scaled this one and this one to one. Either of those is fine. What's inappropriate would be to compare these on different scales. You can see that these are identical when on the same scale, and these are identical when they're on the same scale.
Q. Can any scale be used?
A. Yes.
Q. Just important when there is a comparison they be on the same scale?
A. Yes.
Q. With that background on molar ratio, I want to turn to your understanding of what the term approximately 6:2:5:1 means in the construction of how a person of ordinary skill in the art would understand it. Would you turn back to PTX-1 in your binder. I want to turn to column one, sir.
A. Yes, I have it.
Q. And the paragraph that runs -- begins at line 32.
A. Yes, I have it.
Q. Can you just read the first sentence into the record, please?

A. Yes. Co-polymer-1 is a mixture of polypeptides composed of alanine, glutamic acid, lysine and tyrosine in a molar ratio of approximately 6:2:5:1, respectively.

Q. Do you have an opinion, sir, how a person of ordinary skill in the art would understand just the portion of the phrase 6:2:5:1?

A. Yes, I think a person of skill in the art would understand, because those are whole number relationships that they have errors associated with it, with the numbers or, or what we would call a range that they are not precise. If the numbers were precise, it would be 6.0 or 6.00 to 2.00.

So when we see something that says 6:2:5:1, we know that these are values that are probably associated with what we call experimental error or a range of values.

Q. How many significant figures are used in 6:2:5:1?

A. In each case, one significant figure is used.

Q. How does that play into the analysis of the scope of the term a person of ordinary skill in the art?

A. Well, since it's only one significant figure, one knows that it probably encompasses the rounding range of each of those whole numbers.

Q. What is a significant figure, sir?

A. A significant figure is the value with which you actually know the number. So if you, if you have six eggs, you know it very precisely, can say 6.000, but you wouldn't.

If you do a calculation where you take approximately something, some number and approximately some other number, and divide it on a calculator, you can get ten decimal places on your calculator, but it means absolutely nothing.

So a person of skill in the art has to use a judgment about significant figures. And the rule of thumb is that the number that has the fewest significant figures controls the accuracy and precision of the values.

Q. Do you know, sir, in approximately 1994 what level of precision one could generally -- what was generally reported for amino acid analysis?

A. Yes, I do.

Q. What was level of precision, sir?

A. The level of precision was generally in the range of ten to 20 percent.

Q. If you could turn to PTX-558 in your binder?

A. Yes, I have it.

Q. Do you recognize this document, sir?

A. Yes, I do.

Q. What is it?

A. It is a paper that reports an effort to determine how accurately amino acid analyses could be made.

Q. If you could turn to the table two on page 54 of the paper, I want to focus on the ninhydrin amino acid analysis column do you have it, sir?

A. I do.
Q. What level of precision or average standard deviation is reported here for the ninhydrin amino acid analysis in 1989?
A. These are hydrolysis reactions of a known protein sequence. And intermediate and high refers to the amount of material that was hydrolyzed in order to get these values. The values that are highlighted are 26.4 and 20.0.
Q. And is that consistent with your understanding of the level of precision that was available on this type of analysis at the time?
A. I think so. I said about ten to 20 percent.
Q. If we go to table three, pull up the same ninhydrin column. What is this report, sir?
A. This is a report for sample that is just like the other sample, except instead of sending it to laboratories where they hydrolyzed it and did the analysis, it was a pre-hydrolyzed sample. And then they were all analyzed. And the values given here for the smaller or the intermediate size sample, and the larger sample, I think the larger sample was five micrograms, is looks like 149, but it must be 14.9 and 11.4.
Q. Sir, how would the level of precision available for amino acid analysis affect the person's interpretation of the term 6:2:5:1 under the '808 patent?
A. Well, it tells a person that those numbers cannot be more precise than the experiments that are used to form them.

Q. Is that consistent or inconsistent with your opinion about the scope of 6:2:5:1?
A. I believe it's consistent with my opinion.
Q. Can you explain why?
A. Yes, because numbers are the values that we use to represent our data, but our data rely upon the experimental methods that we use to obtain the data. And we often have -- often -- we always have experimental error in the work that we do. So there is variance, variation from experiment to experiment. We typically will run an experiment three times try to figure out what's the range of values that we see. And we try to express our data as realistically as we can, given that range of variations that seems to be inescapable whenever you do experiments.
Q. Take the slide down, please. Sir, I want to turn then to the word approximately and approximately 6:2:5:1. How does that word, in the Court's construction in the '808 patent, impact your understanding of the scope of approximately 6:2:5:1?
A. We know from the whole number values of 6:2:5:1 that these must be a single precision values, single significant figure precision values. When it says approximately 6:2:5:1, it must mean that the range is a little bit broader than just the rounding range.
Q. Are there any references cited in the '808 patent that help

you understand the scope of approximately 6:2:5:1?
A. Yes. I think a person of skill in the art would have looked at the '808 patent, any of those that have the same specification, and seen that the Teitlbaum co-polymer-1 compounds were included as examples of co-polymer-1.
Q. Let's go back to PTX-1 just to see what you're pointing to. If we could turn to PTX-1, column one and look at the paragraph begins on line 23. We called it up on the screen, Dr. Gokel.
A. Thank you.
Q. If you could just read the first two sentences into the record?
A. Yes. Co-polymer-1 was developed by Doctors Sela, Arnon, and their co-workers at the Weizmann Institute, Rehovot, Israel.
Q. And the next sentence, please?
A. It was shown to suppress EAE, and the reference given is the European Journal of Immunology in 1971, volume 1242, and United States patent 3849550.
Q. Based on this passage, would a person of ordinary skill in the art understand that these references helped to define what is co-polymer-1?
A. I believe they would.
Q. If we could your Honor to PTX-499 in your trial binder.
A. I have it.
Q. Do you recognize this paper, sir?

A. Yes, I do.
Q. What is it?
A. It is a paper by Teitlbaum and co-authors called suppression of experimental allergic encephalomyelitis by a synthetic polypeptide.
Q. Is this the paper that's cited in column one of the '808 patent?
A. It is.
MR. WIESEN: Your Honor, plaintiffs offer PTX-499 into evidence, if it's not already in the record.
THE COURT: Any objection?
MR. ANSTAETT: No objection.
MR. DOYLE: No, your Honor.
THE COURT: Admitted.
(Plaintiff's Exhibit 499 received in evidence)
Q. Thank you. Could we look at section 2.3.1 on page 243 of this paper?
A. Yes.
Q. What does it, what does it describe, sir?
A. It describes the synthesis of co-polymer-1, saying that it was prepared by the N-carboxyandhydrides method. It gives the four amino acids that we mentioned before in protected form. And it says the polymerization was carried out using diethylamine as initiator, deblocking or removal of the gamma benzyl group with hydrogen bromide acidic acid. That's the

procedure we've just been through a couple of times. That's the synthesis of one batch.

And then it says, a second batch of this polymer was prepared in an identical manner.

Q. Does it indicate that there the results from those two batches are listed in table one?

A. Yes. It then shows the results in table one.

Q. Could we look at table one on the same page, 243?

A. Certainly.

Q. What is this table titled?

A. The table is titled composition of co-polymer-1.

Q. Does the report molar ratio for the two batches of co-polymer-1 in the Teitlbaum 1971 paper?

A. Yes. It does. And the penultimate and final columns of this paper it shows the molar ratios for these two batches that the paper says were prepared in an identical fashion.

Q. If you could just read into the record the molar ratio for batch one in the Teitlbaum 71 paper?

A. Yes, for the amino acid alanine, glutamic acid, lysine and tyrosine respectively. The molar ratio is given as 6.0, 1.9, 4.7 and 1.0.

Q. And what's the reported molar ratio for batch two in the Teitlbaum 1971 paper PTX-499?

A. For the same four amino acids in the same order, it's 6.7. 2.1, 4.2 and 1.0.

Q. Sir, would a person of ordinary scale in the art have considered batch two to be a batch of co-polymer-1?
A. Yes, a person would have.
Q. Why?
A. Because it is stated to be that in this paper. It is stated to be that in the patent, and the authors of this paper that we're looking at right now said that these two batches were prepared identically. So a person of skill in the art would recognize that these are experimental variations that, as I said, occur in all of our experiments.
Q. And would it, would a person of ordinary skill in the art have considered 6.7, 2.1 to 4.2 to 1.O to be approximately 6:2:5:1?
A. Well, since the patent says that this is co-polymer-1, a person of skill in the art would have to recognize this as a valid molar ratio within that framework.
Q. Now, could a person of ordinary skill in the art use batch two to determine what percent difference from 6:2:5:1 would be approximately 6:2:5:1?
A. Yes, I think so.
Q. Could we have the next slide, please. Have you done that calculation, sir?
A. I have.
Q. Could you explain what you're showing here on the slide 71?
A. Yes. I've asked the question, what is the variance, what's

the difference between the molar ratio that has been expressed and what was actually observed experimentally. And to try to keep the analysis simple, I simply asked the question how different is each of these numbers from the whole number, .7 1.8 and 0. The total of all those differences is 1.6, and that's about 12 percent difference when you divide by 14.

Q. Why do you have to divide by 14, sir?

A. Because the molar ratio scale that we're using is 14.

Q. Would it be appropriate to simply say that the difference is 1.6?

A. Well, you could say that the difference is 1.6, but it wouldn't have any particular meaning, I think to someone because the question is how does it differ from the molar ratio, not what -- in other words, you'd have to ask the question what exactly is 1.6.

Q. Thank you, sir.

If we could turn to PTX-26 in your trial binder?

A. 26?

Q. 26.

A. I have it.

Q. Do you recognize this document, sir?

A. Yes, this is U.S. Patent 3,849,550.

Q. Is this the other reference cited in column one of the '808 patent that we looked at earlier?

A. Yes, along with Teitlbaum article we were just discussing.

Q. If we could pull out column two, lines 19 to 26. Do you understand, sir, that this is a discussion of co-polymer-1?
A. Yes, I do.
Q. What's the basis for that conclusion?
A. Well, it states here that it is a preferred copolymer according to the present invention.
Q. And what amino acids are reported to be in this copolymer?
A. The same ones that we've been talking about, alanine glatiramer acid, lysine and tyrosine.
Q. Would a person of ordinary skill in the art understand this batch to be co-polymer-1 as the term as used in the '808 patent?
A. Yes, it is, designated that within this patent.
Q. What is molar ratio reported here?
A. The molar ratio is 6:2:4.5:1.
Q. Would a person of ordinary skill in the art understand 6:2:4.5:1 to be approximately 6:2:5:1?
A. Yes, that would be essential within the understanding of the 6:2:5:1 molar ratio, because this is stated to be co-polymer-1.
Q. Thank you. If we could take that down, please.

Now we've looked at the scope of approximately 6:2:5. 1 have you analyzed whether Mylan's proposed ANDA product would have a molar ratio of approximately 6:2:5:1?
A. Yes, I have.

Q. And what's your opinion, sir?
A. My conclusion is that the Mylan products have a molar ratio of 6:2:5:1, approximately.
Q. Could you turn to PTX-325 in your binder?
A. Yes, I have it.
MR. WIESEN: If we could actually go to the next slide, your Honor, try and speed things up a little bit, we've prepared, preprepared some slides that have some of the molar ratio data so we can try and move things along as we go through the documents.
THE COURT: All right.
Q. If that's okay, Dr. Gokel, if it's okay with you, we'll try and work off this screen and off the slide. We're on slide 72?
A. Say you want to work off the screen?
Q. I think that would be easier.
A. Okay.
Q. If we can do it. So if we look at just for the record, in PTX 325 MYL 1050, is -- reports results a certificate of analysis with results on GMA/001/009; do you see that, sir?
A. Yes, I see it here at the top.
Q. Can you read the molar ratio that's the molar fraction that's -- excuse me, let me start again. Can you read the molar ratio that's reported for that batch into the record, please?
A. For the amino acids, glutamic acids, alanine, tyrosine and

lysine, the molar fraction that's reported is .144, .427, .092, and .6.

Q. And if we turn just for the record to MYL 68, we have a certificate of analysis for GMA/002/09, and do you see the reported molar ratio of amino acids on this pull out from that page sir?

A. Yes, I see it.

Q. And what's the reported molar ratio?

A. For the same four amino acids in the same order, it's .148, .432, .092, and .328.

Q. For the record, if we turn to MYL 1079, that has a certificate of analysis for GMA/003/009, and row eight also reports molar ratios. If you could read those into the records sir?

A. Yes, for glutamic acid, alanine and lysine, it's 402 -- I'm sorry, little dyslexic, .142, .440, .092, and .327.

Q. Thank you, sir. And what scale would you say that these molar ratios are reported on?

A. These are mole fractions that are reported on a scale of unity.

Q. By scale of unity, you mean they all add up to one?

A. Yes.

Q. Now, sir, would a person of ordinary skill directly compare these mole fractions to 6:2:5:1?

A. If you mean by direct, are numerically comparable, the

answer is no. But it's just a numerical manipulation. You would multiply and you could compare them directly.

Q. Have you done an analysis and detail of the molar ratio and how you could compare it for GMA/001/09?

A. Yes, I have.

Q. Could we have the next slide, please? What do you have here on slide 73?

A. I have our four amino acids, alanine, glutamic acid, lysine and tyrosine. The mole ratio expressed in the '808 related to patent to 6:2:5:1, and this is the mole fraction, molar fraction. These numbers express, these exact numbers express as mole fraction, and this is the lot GMA/001/09, and it compares with these numbers.

Q. And so you're indicating, sir, that you would compare the 3rd and 4th column on slide 736:2:5:1 on a scale of one and the lot GMA 001/009 on the scale of one, is that right?

A. Yes. I'm saying that the numbers in the 3rd and 4th columns are comparable and they are the same scale.

Q. And so would a person of ordinary skill in the art consider those numbers to be approximately the same?

A. Yes.

Q. Now, if you wanted to compare on the scale of 6:2:5:1 or the scale of 14, what would a person of ordinary skill in the art do to the reported mole fractions for GMA/001/09?

A. Well, if you want to compare these numbers, that is the lot

GMA numbers, with the 6:2:5:1 ratio, all you need to do is get it on the same scale, so you just multiply by 14.

Q. And what results do you get, sir, on the scale of 14 for the Mylan log?

A. Well, the numbers that result are 5.98, 2.02, 4.70 and 1.29.

Q. And in your opinion, sir, would a person of ordinary skill in the art consider those numbers to be approximately 6:2:5:1?

A. Yes.

Q. Have you prepared some graphs and graphics to illustrate how you compare these numbers?

A. Yes, I have.

Q. Could we have the next slide, please? What do you have here, on slide 75?

A. The data, the data as mole fractions are shown here at the bottom with colored lines to indicate the proportion, and this is on a scale of one, and this is perfectly valid, but it's hard to see. And it's blown up here, but even so, it's hard to see. So I've simply multiplied by 14. I have these two stacked plots that I can compare, and you can see that they are very very similar.

Q. And, sir, why is it important that the results be on the same scale to compare them?

A. If they're not on the same scale, it's a mathematical distortion.

Q. Have you also created some pie charts to allow -- to show the comparison between exactly 6:2:5:1, and Mylan's molar ratio of this batch?
A. Yes, I have.
Q. Could we have the next slide, please. What does this slide 76 show?
A. This, in essence, shows exactly the same thing. It's represented mathematically a different way as a pie chart, because the entire molecule or ensemble is represented as a whole. And when we put these on the same scale, we can see the correspondence of the various sliced sizes.
Q. And in your opinion, sir, are these molar ratio proceeds approximately the same?
A. Yes, they are.
Q. Could we have the next slide, please. Now, you done a similar analysis, sir, for Mylan lot GM/002/09, and Mylan lot GMA 030309?
A. Yes, I have.
Q. You did you reach a conclusion whether Mylan lot GMA 00209 is approximately 6:2:5:1?
A. Yes, I did.
Q. And what's your opinion, sir?
A. In each of these cases, I believe it is in the molar ratio approximately 6:2:5:1.
Q. Just to make sure the record is clear, did you do that

analysis as well for Mylan lot GMA/003/09?
A. Yes, I did.
Q. And what conclusion did you reach?
A. That it is approximately 6:2:5:1.
Q. And, sir, based on this analysis, have you reached a conclusion whether you believe Mylan's drug substance would be co-polymer-1 as the Court has construed the term if they followed the synthetic process in their ANDA?
A. Yes, I believe it would be co-polymer-1.
Q. Thank you, sir. I want to turn quickly then to Mylan drug product lots. If we could have the next slide.
MR. WIESEN: And, your Honor, we've prepared the same sort of graphic rather than trying to run through the certificates of analysis. I believe Dr. Grant actually put them into evidence, looking at the molecular weight terms. Just for the record, WV-901 is the certificate -- sorry PTX-300 is a certificate of analysis for WV901. PTX-312 is a certificate of analysis for batch WV902 and PTX-313 is a certificate of analysis for batch WV 903.
Q. And, sir, if we could just read into the record the molar ratio for the 1st, 2nd and 3rd drug product batches Mylan has in its ANDA?
A. Yes. For 901, for glatiramer acid alanine, tyrosine and lysine, the molar fractions are .137, .462, 090, .311. For the 902 batch in the same order for the same amino acids, they are

.146, 0.463, .088, .304.
Q. Could you just read the last record?
A. Yes.
Q. The last batch into the record as well, please?
A. Yes. For the last batch, batch 903, for the same amino acids in the same order, it's .144, .464, .088, .305.
Q. And, sir, have you conducted a similar analysis to determine whether Mylan's drug product batches have a molar ratio of approximately 6:2:5:1?
A. Yes. I believe they have a molar ratio of approximately 6:2:5:1.
Q. And based upon that analysis, do you have a conclusion or an opinion concerning whether Mylan's proposed drug product would be co-polymer-1 as the term has been construed?
A. Yes, I believe it to be co-polymer-1.
Q. Finally, do you have an opinion whether if Mylan followed the synthetic procedures outlined in their ANDA, the compound that they would make would be co-polymer-1 as the term is used in the patents-in-suit?
A. Yes, I believe it would be.
Q. Were you here, sir, for Ms. Bloodworth's opening on behalf of Mylan?
A. Yes, I was.
Q. And did you hear her talk about the need to normalize or set tyrosine to one when creating molar ratios?

A. Yes, I did.
Q. Do you have an opinion whether that sort of procedure would be appropriate when comparing to the molar ratio of approximately 6:2:5:1?
A. Yes, I do.
Q. What's your opinion, sir?
A. I don't think that procedure is necessary, and it's inappropriate unless it's on the same scale.
Q. Could you explain what you mean by that?
A. Yes. If you, if you normalize to one, then it accordingly changes the other values, perhaps reducing or perhaps raising, giving you a scale that's different from 14 or different from one. So a direct comparison simply isn't possible.
Q. When you normalize, do you change the relative percentages in a mixture?
A. You don't change anything about the mixture. The mixture remains. It's the mixture that's determined experimentally. What you're doing is a mathematical manipulation. And for it to be valid, you need to be comparing, forgive me for saying this, apples to apples.
Q. Sir, I want to go to the next slide. I want to go -- actually, could we have the next slide, please. Have you created a slide with your pie chart to explain this point in an individual way?
A. Yes, I've used pie charts here because pie charts encompass

the whole. And so if we have a total scale and look at the proportion, we can see that they are identical. Because this is the same lot. This is just bigger than this. But if we say that there is, there is less of something or more of something, and we want to compare it with our scale here, or our scale here, we need to be sure that it's on the same scale as either this or sorry -- this is, this is the same batch. We need to be sure that it's on the same scale as the 14 so that the comparison is valid.

Q. And I want to return, sir, then to the polypeptide chain of 70 amino acids that we started the discussion with.

A. Yes.

Q. And this is the polypeptide that you created that has the ratio of exactly 6:2:5:1, is that right?

A. Yes, that's correct.

Q. And did you create a similar polypeptide chain using Mylan proposed molar ratio?

A. Yes, I did.

Q. And what's this on the bottom of slide 81?

A. This is a schematic representation just as made above, of Mylan's drug substance, except instead of having 30 alanines, ten glutamic acid, 25 lysines and five tyrosines, we have replaced one of the lysines by a tyrosine. So we now have 30 alanines, ten glutamic acids, 24 lysines, and six tyrosines. So there's been one change of one amino acid out of the 70, and

that's the difference between exactly 6:2:5:1, and Mylan's drug substance here.

MR. WIESEN: Your Honor, that's the end of the discussion about Mylan product. It might be a good breaking point?

THE COURT: Okay. How longer do you expect the direct to be tomorrow?

MR. WIESEN: Should be an hour or less, I believe.

THE COURT: All right. I am sorry we have to break early today, but I'll see everybody at 9:30 tomorrow morning. Thank you, Dr. Gokel.

THE WITNESS: Thank you.

MR. WIESEN: Thank you, your Honor.

THE COURT: Have a nice evening.

(Adjourned to September 9, 2011 at 9:30 a.m.)

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